THE ENZYME TREATMENT FOR CANCER

By

WILLIAM SEAMAN BAINBRIDGE, A.M., Sc.D., M.D.

Scientific Report
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SURGEON, NEW YORK SKIN AND CANCER HOSPITAL; HONORARY PRESIDENT, FIRST INTERNATIONAL CONGRESS ON CANCER; SECRETARY, COMMITTEE ON SCIENTIFIC RESEARCH, NEW YORK SKIN AND CANCER HOSPITAL.

IN a previous communication—"Trypsin in Cancer, a Preliminary Statement," published concurrently in the *British Medical Journal* and the *New York Medical Journal*, March 2, 1907—I expressed the determination of giving to the "enzyme treament," as outlined by Dr. John Beard of Edinburgh, a thorough, scientific test, in a sufficiently large number of cases and over a long enough period of time, to warrant some claim to finality when conclusions were drawn. It was pointed out that many months must needs elapse before such a test could be reported in full. Now, after an interim of more than two years since the "preliminary statement" was made, and full three years since I began to employ the enzyme method, it would seem that a final report may be offered which will meet the requirements of what may be called a "fair test."

No explanation need be offered to those who have read the leading medical journals, American and European, during the last four years and more for having given to this method of treating cancer the fair trial which its originator so earnestly desired.

Dr. Beard succeeded in arousing the interest of a goodly number of the members of the profession, both in Europe and America, as is shown by the fact that more than one hundred articles have been written upon the subject, and that five hundred physicians, out of more than three thousand to whom letters of inquiry were sent by me as Secretary to the Committee on Scientific Research of the New York Skin and Cancer Hospital, have employed the method. Whatever might be one's opinion concerning the theories upon which the so-called "trypsin treatment" was based, there seemed quite enough of possible value in the method to warrant its trial. Furthermore, through the overzealous influence of certain medical writers for the lay press and a few premature enthusiasts within the ranks of the profession itself, the method was heralded far and wide, and patients soon began to make the demand that it be tried in their case. Hoping that it might prove, if not the boon which it had been pronounced, at least a helpful adjuvant, and believing that it would do no material harm, we proceeded with the test, report of which is now offered.

It is but just to all concerned—to Dr. Beard, who proposed the method; to Mr. B. T. Fairchild, who so skillfully prepared and so generously supplied the materials; to the physicians and surgeons who cooperated with us; to the laboratory workers; to the bedside attendants, and to the patients themselves—to say a word concerning the difficulties involved in giving to a non-surgical method for the treatment of cancer a thorough and final test.

The New York Skin and Cancer Hospital furnished ample clinical material from which to draw a large proportion of the cases in which the method was tried. To employ it only in advanced, irremovable, and inoperable cases was simple enough, but

such cases do not give a sufficient basis for a complete trial. The surgeon, who must look upon the matter not as a "pure scientist," but as a clinician and a humanitarian, cannot bring himself voluntarily to subject a patient with cancer in an early stage, when it is amenable to complete removal by surgical intervention (certain local superficial growths in the judgment of some being excepted), to experimentation with *any* non-surgical method, no matter upon what scientific basis it may be exploited. Consequently such a method may be tried in early cases only where, despite the surgeon's earnest advice, operation is positively refused by the patient. As will be seen, a number of cases of this class are on our list.

An enormous amount of time and patience and much money were necessary in following out the details of the treatment. Inasmuch as it of necessity extended over weeks and in some instances months, it was not feasible in all cases to care for the patients in the hospital, the individuals themselves not infrequently objecting to being so long away from home. Under these circumstances, when the patient could not afford the expense, it was necessary for us to furnish medical attention and employ trained nurses to administer the treatment and carry out the régime in the home after the patient's discharge from the hospital. To follow up the records in all cases from week to week and from month to month in such a manner as to render possible an accurate report of each, meant, in many instances, tracing the patient from tenement to tenement, sometimes from city to city. Innumerable obstacles were encountered at every turn. We endeavored, however, to meet these as they arose, to follow the régime outlined as closely as was feasible according to the exigencies of the individual case, and to keep as accurate data as possible in each instance. We believe we have been reasonably successful, despite the many difficulties, yet with all our care we were unable to follow some of the patients to the end, or to the present time.

In this connection I wish to extend sincere thanks for their hearty cooperation in the work to the following: Dr. Martha Wollstein, Pathologist to the New York Skin and Cancer Hospital; Dr. James Ewing, Professor of Pathology, Cornell University Medical Department; Dr. F. B. Mallory, Professor of Pathology, Harvard University Medical School; Dr. S. Elizabeth Finch, Assistant Pathologist to the New York Skin and Cancer Hospital; Dr. F. M. Jeffries, Pathologist to the New York Polyclinic Medical School and Hospital; Dr. F. D. Jessup, of the Department of Pathology, College of Physicians and Surgeons; Dr. E. E. Smith, Pathologist to Fordham Hospital, and others, for their valuable assistance in the laboratory phases of the work; Dr. J. Douglas Malcolm, of the staff of the New York Skin and Cancer Hospital, for his assistance in administering the treatments and following up the cases after their discharge from the hospital; Dr. Loy McAfee Inghram, Statistical Secretary to the Committee on Scientific Research of the New York Skin and Cancer Hospital, for accurate collation of scientific data, and the various graduate nurses who have so carefully executed the details of the regimen in the homes of many of the patients. Especially do we wish to express our appreciation of the generosity of those who have been kind enough to contribute funds toward covering in part the necessary expense entailed in the successful conduct of the work.

THE METHOD.

It is not necessary for the purpose of this report to review the interesting, if not generally accepted, embryological theory of the cause and development of cancer upon which Dr. Beard founded his method of treatment. The "irresponsible trophoblast" does not concern us here. Those not familiar with the theory can easily become so by reference to Dr. Beard's printed works.

Suffice it for our purpose to say, that at all times during the trial of the enzyme treatment I have been in close touch with Dr. Beard, and have followed the essentials of his method in all respects save one. When I first began to test the treatment Dr. Beard advocated its use in all cases after operation for the removal of cancer, whether primary or secondary, and in all inoperable cases. In this I readily concurred. When, however, at a later date, he modified his views, and opposed the removal of any "living cancer," declining to accept as a scientific test any case in which there had been previous operation, of course I demurred. This demand was met, however, as we have already seen, in cases where operative intervention was positively refused. We feel, therefore, that while the method has not been tried exclusively in such cases, we have been able to test it in a sufficient number to meet this requirement with justice to Dr. Beard's modified views.

In addition to the use of the enzymes, many details of management were urged by Dr. Beard. His various suggestions were incorporated by me in the directions for the "full regimen," and were employed in our test, with modifications to suit the needs of the individual case. In the reports and the table of cases which follow, unless otherwise specified, this regimen was executed in every instance, a copy of the directions being given to each one who administered the treatment.

DIRECTIONS.

1. *Physical Examination*, accurate and complete, made upon commencement of the treatment.

2. *Records* of each case, accurately and fully taken *daily*, with *weekly* records of the condition of the urine, blood, and, if possible, blood pressure, and weight. Both subjective and objective symptoms to be carefully noted.

3. *Diet*, wholesome and nourishing, with very little salt and no acids. Large quantities of water to be taken by the patient.

4. *Exercise* moderate.

5. *Hygienic surroundings* as good as possible, with abundant fresh air.

6. *Oral Treatment*: (1) *Holadin*, 1 capsule t.i.d., one hour before meals. (2) "*Pepule*" *oxgall compound*, 1 to 2 pills at night, according to requirements (to give tone to the bowels).

7. *Local Treatment: Lotio Pancreatis.*—To the quantity required for a single application, add an equal volume of freshly distilled water (unless ordered to be employed undiluted) and apply freely. Use twice daily, flushing the surface carefully with boiled water previous to renewal of solvent.

8. *Hypodermatic Treatment:* (1) *Injectio Trypsini* (Special XX). Begin with ten minims daily, increasing five minims each day until some marked reaction takes place, or until two ampoules (20 minims each) are being taken each day.

(2) *Injectio Amylopsini.* When the trypsin injections have been increased to 40 minims daily injections of amylopsin are then begun on alternate days with trypsin, never on the same day. Commence with ten minims, increasing five minims each day until the maximum dose is reached, viz., 40 minims of trypsin one day and 40 minims of amylopsin the next.

Before making the injections apply ethyl chlorid to the surface to be injected (preferably over the buttocks), or inject 1/10 grain eucaine, then inject the trypsin or amylopsin into the deeper subcutaneous tissues, not into the muscles.

Note 1. The greatest care, cleanliness, and nicety in every detail must obtain.

Note 2. The doses must be regulated with careful regard to the reactions observed.

Note 3. The contents of the ampoule must be used *only when freshly opened.*

Note 4. The ferments are destroyed by antiseptics; care must be taken therefore not to render them inert by contact with such substances.

Note 5. If there is any local irritation from the injection, despite the greatest care, dilute with equal parts of distilled sterilized water before injecting, or with equal parts of sterilized normal salt solution.

Note 6. The general condition of the patient must be given careful attention. As little narcotic medication should be given as possible, tonics and pre-digested foods, if indicated. Elimination by bowels, kidneys and skin is of the utmost importance.

Note 7. The treatment, after well started, is said to have a definite control over pain. Over-drugging should be avoided in order that this claim may be carefully studied in relation to the cases.

Note 8. Injections of amylopsin should not be given while the patient's stomach is empty, as the tendency to nausea is increased under such circumstances.

Note 9. If irritation results from the introduction of the entire injection in one locality, this may be overcome in the following manner: Introduce the needle tip into the tissues, inject a portion of the material, withdraw slightly, introduce in another direction and inject another portion, and so on until the entire amount is inserted into the subcutaneous tissues in "puddles" at some distance from each other, but with one common point of puncture. By taking this precaution the tissues will not be over-distended, and the tendency to irritation will be lessened. The needle should be inserted obliquely so that the material will not escape in part through the puncture point.

Abscess formation, so-called, was noted in some cases, and has been reported by a number who have employed the method. Real abscesses are due to (1) faulty technique; (2) localization of infection in cases where there is a general condition of sepsis from absorption of broken-down material; (3) from a complicating infection such as tonsilitis or la grippe. The so-called "trypsin abscess," on the other hand, has been shown by examination of the material to be not a true abscess, but unabsorbed trypsin solution with some broken-down tissue cells. After prolonged treatment the tissues in some cases fail to absorb the material which, in time breaks down, is discharged, and a sinus is left for a while.

THE MATERIALS.

We are indebted to Mr. B. T. Fairchild for the materials employed. They consist of the following : (1) Holadin capsule, a pancreas gland extract containing all the pancreas enzymes—trypsin, amylopsin and lipase—and the milk-curdling ferment. This is given to aid digestion. (2) "Pepule" oxgall compound, which contains inspissated oxgall, extractum pancreatis, and extract of nux vomica. This gives tone to the bowel and aids in elimination. (3) Lotio pancreatis, a glycerin extract prepared directly from the fresh gland and carrying in solution the entire soluble gland constituents. This solvent of broken-down tissue is applied topically to the ulcerating surfaces. (4) Injectio trypsini, a glycerin extract of trypsin, which, according to Beard, was supposed to "kill" the cancer cells. (5) Injectio amylopsini, a glycerin extract of amylopsin, which was thought to "digest" the dead cancer cells.

The first pancreas injections were made of a proteolytic power qual to 2 per cent. of trypsin, and adopted in consequence of a strength or "percentage" of trypsin, first extemporaneously prepared and used by Beard and others. The medium, 60 per cent. glycerin, had already been found to meet the requirements, containing the enzymes of the fresh pancreas extract in an active and sterile condition. This, however, necessitated preliminary dilution in making the injection ready for use. Gradu-

ally clinical experience warranted an increase in tryptic power, until finally this desideratum could be achieved only by a more aqueous medium, and consequent reduction to 20 per cent. glycerin. This lower content of glycerin afforded the advantage of increase of trypsin content and increase of dosage, as found in the ampoule.

The various injections of trypsin furnished for our use were identified for convenience of record as follows: "Regular," 60 per cent. glycerin, equal to 2 per cent. trypsin (dry); "Fortified," 60 per cent. glycerin, double the strength of the "regular;" "Special," 20 per cent. glycerin, double the strength of the "regular;" "Special XX," 20 per cent. glycerin, four times the strength of the "regular" (this was used in most our cases); "Special Quadruple X," 20 per cent. glycerin, six times the strength of the "regular" (prepared especially for this test, and said at the time to be the strongest it was possible to make).

Injections of amylopsin of corresponding strengths were furnished us. The 20 per cent. glycerin amylopsin injection presents parallel advantages with the 20 per cent. trypsin injection, in increased potency, and in available volume of dosage without dilution. Thus, twenty minims of the 20 per cent. glycerin "Special" carries an enzyme potency corresponding to a sixty minim injection composed of twenty minims of 60 per cent. glycerin solution from an ampoule, with forty minims of diluent—sterilized water.

Having noted the strengths of the injections, it will be seen from the cases detailed later, how much stronger were the injections used in many of our tests than were those employed in the cases reported by a number of writers during the earlier months of the history of this method. The idea entertained by many at first, to the effect that only moderate doses of weak solutions of trypsin could be tolerated, was proved entirely erroneous in our experience. In many cases we were able to give daily two or three ampoules (twenty minims each) and in several instances 100 minims for days at the time of the "Quadruple X" solution with no untoward effects. From this it will be seen how absurd were some of the earlier claims of "cures," as well as of the strange symptoms and "terrific" results from the small doses employed.

A careful study of the blood and urine in a certain number of cases was made, under my direction and with valuable suggestions from Dr. Martha Wollstein. For the painstaking execution of this work, and the careful recording of the findings, credit is due to Dr. S. Elizabeth Finch.

THE BLOOD IN MALIGNANT DISEASE

It may not be amiss before considering the blood examinations to review briefly the opinions of some of the leading writers concerning the blood in cancer.

Malignant disease is given by Emerson as one of the most important causes of anemia. It is remarkable, however, how long the blood presents an almost normal picture before the beginning of the anemia, which then progresses rapidly and parallel to the cachexia. In some cases of cancer there may be no amemia. Cabot gives the percentage as about one-fourth the cases. V. Limbeck (cited by Emerson) says that blood normal qualitatively is common and perhaps the rule, even in advanced cases; that in cases with dessicated tissues there may be even a rise in the count; and in advanced cachectic cases without hemorrhage there is seldom diminution in the red count, and then it is not extreme. Severe anemias occur in cases associated with frequent hemorrhage, e.g., cancer of the stomach and uterus; severe anemias occur from mechanical effects, e.g., cancer of the digestive tract; extreme grades of anemia may be caused by the cancer toxin, e.g., cases approximating the picture of pernicious anemia—diagnosed as cancer perhaps only at autopsy. Anemia when present is

usually of the secondary type. The common picture is that of the so-called "pseudo-chlorosis carcinomatosa." According to Cabot, in one-half the cases the anemia is of the chlorotic type, while one-fourth show reduction in both count and hemoglobin. Grawitz claims that the cancer produces a plasmotrophic poison—that is, that which may affect the blood, or the blood plus the body tissues, or the tissues without the blood, producing in some cases merely degenerations of the red cells; in other cases an anemia parallel to the cachexia; in still other cases a marasmus of the highest grade yet with the blood only slightly affected.

In the cases of anemia the hemoglobin is generally conceded to be first reduced; Emerson says always, though modifying the statement that when normal, the red blood cell count is above normal. He gives the average in long standing cases as 68.5 per cent., in more severe cases as 57.5 per cent. Cabot gives the average per cent. as 58. Ewing says that the first sign of affection of the blood in cancer of the stomach is seen in the falling hemoglobin, which has been found considerably reduced in many of the cases with normal or nearly normal red cells. Low percentages of hemoglobin are found in visceral cancer. The lowest are found among the cases of cancer of the stomach, intestines and uterus. Emerson gives forty, twenty-eight, and forty per cent. respectively as found in three out of ten cases of cancer of the intestines. The hemoglobin is said to be more reduced in cases of sarcoma than in other cancers, the average being about fifty per cent., while cases below ten per cent. have been reported. From the study of his cases, Emerson did not find the blood more abnormal in cases of sarcoma than in other cases. High percentages of hemoglobin are reported in some cases of cancer of the esophagus, where there is concentration of the blood, also, in cases of laryngeal involvement with the presence of cyanosis.

The hemoglobin index is given as lower than one as a rule. Cabot gives the average as 0.65. The index is low even in severe anemias approaching the pernicious anemia type. There are on record at least two cases with an index over one.

Bierfreund states that after operation in cancer cases regeneration of the blood begins at least one week later than would be expected, and never quite regains the percentage it was before operation.

Deformities in size and shape, and degeneration of red blood cells may be absent or may approach the type found in pernicious anemia, though they are rarely as marked. The most common picture is that found in mild cases of chlorotic anemia. The type of nucleated red is usually the normoblast, though megaloblasts in small numbers may be present in the more severe anemias. Very high nucleated red counts may be found in cases involving bone marrow; while in cancer of the stomach in cases simulating pernicious anemia the nucleated reds may be rather rare. The number of red ce ls per cubic cen imeter varies from above normal, when for any reason there is concentration of the blood, to 500,000 reds (Grawitz). Cases with counts under 1,800,000 are · are.

The blood in cancer is hydremic, with reduced albumen. Metabolism experiments indicate an abnormal destruction of tissue proteid, the evidence of a circulating toxin. The specific gravity of the blood is low. The plasma is rich in sugar, even as rich as in diabetes. The coagulation is normal or retarded unless sloughing or inflammal tion be present, in which case it may be rapid. The fibrin network is usually norma- (Emerson).

The total leucocyte count varies from a leucopenia to a marked leucocytosis, depending upon the position of the cancer, the presence or absence of complications, and the occurrence of hemorrhages. According to Emerson it also depends, though subject to g·eat variations, upon the size of the cancer, including of course the metas-

tases. The larger and faster the tumor grows the greater is the leucocytosis. He also states that there is a moderate leucocytosis in about sixty per cent. of all cases; that after operation the leucocytes drop, and that their subsequent rise may indicate a recurrence even before it can be found physically. Grawitz considers that leucocytosis is coincident with the softening of the tumor mass. In a large proportion of carcinoma cases and in a rather smaller proportion of sarcomas the cachexia is unaccompanied by hyperleucocytosis unless there is a distinct local inflammation, necrosis or hemorrhage. The existence of a marked hyperleucocytosis in the course of a cachexia should lead to a search for one of these complications (Ewing).

Emerson gives a slight leucocytosis (11,000) for cancer of the breast. He says that little value can be placed on the count in cancer of the stomach, though there is a leucocytosis in over one-third of the cases, and in those without it the digestive leucocytosis is often absent (in 82 per cent. of 144 cases—DaCosta). Low counts below 4,000 he states as not rare—his highest was 52,800. The statement that the rapidity of growth controls the count was not corroborated in his cases. Ewing gives the grade of leucocytosis in gastric cancer as usually not high; but, since in low states of nutrition the leucocytes are usually low, the presence of 10,000 leucocytes has more significance than in health. The majority of abnormal cases show between 10,000 to 20,000 white cells per cubic centimeter. Higher numbers are usually the result of complications. Cancers of the kidney, thyroid and some of bone, show high leucocyte counts. In uterine carcinoma hyperleucocytosis is usually seen only when there is extensive ulceration. Mycmas lead to hyperleucocytosis only as the result of extensive hemorrhages (Simon). There is no leucocytosis in epithelioma of the skin. Leucocytosis is even more common in sarcoma than in carcinoma.

As a rule, leucocytosis means an increase of the polymorphonuclear neutrophiles, but in some cases it is the lymphocytes that are increased (Emerson). In sarcoma the leucocytosis is more apt to be due to an increase in the lymphocytes. This qualitative change may be present when there is no increase in the total number of leucocytes. There are on record several cases of sarcoma associated with lymphatic leukemia. As the more malignant tumors obliterate lymph paths, some inference regarding prognosis may be derived from the presence or absence of lymphocytosis in these cases (Ewing). In most splenic tumors there is a relative or absolute lymphocytosis (Müller and Rieder and Weiss, cited by Ewing).

In malignant disease eosinophilia apparently occurs in only a relatively small percentage of cases, and when present is usually of moderate grade, i.e., not exceeding seven to ten per cent. (Simon). Occasionally, however, the increase is most remarkable. In the differential diagnosis of carcinoma from pernicious anemia Simon has found that an increase of polynuclear neutrophiles associated with a normal or supernormal eosinophile count is very suggestive of cancer. In septic conditions the neutrophiles are relatively increased and the eosinophiles coincidentally very much diminished or absent altogether (septic factor of Simon). In gastric cancer Ewing gives the eosinophile cells as nearly always present; sometimes increased five to six per cent.

Myelocytes are said to be of not infrequent occurrence. According to Kurpjurweit (*Deutsches Arch.*, Vol. LXXVII) the occurrence of myelocytes in large numbers (4 to 17 per cent.) in connection with the symptom complex of a severe anemia is to be viewed as almost pathognomonic of malignant growth with bone-marrow metastases, even when a primary tumor cannot be found. However, in anemic conditions of whatever origin it is common to meet with a moderate number of neutrophilic myelocytes (Simon).

Simon has found the number of mast cells diminished or entirely absent in some cases of carcinoma of the cervix (septic).

BLOOD EXAMINATIONS.

Blood examinations were made regularly over a period of ten months in a number of hospital and dispensary cases to observe what effect, if any, was produced by the enzyme treatment on any anemia present, or on the white cells of the blood. Leucocyte and differential blood counts were made once a week in the different cases, and hemoglobin tests and red blood cell counts were made as deemed necessary. Upon placing a case on the treatment, in so far as possible, two, preferably three, blood counts were made on two or three successive days preceding the first injection; one count within twelve hours of the first injection, and then one every twenty-four hours or forty-eight hours for the first few days.

Blood examinations were made in thirty-seven cases, but in only nineteen did the observations extend over a period of more than four weeks, the treatment being discontinued for one cause or another, or the patient passing out from under observation.

Of the thirty-seven cases in which blood examinations were made, nine were epitheliomata and the rest carcinomata. There were no cases of sarcoma. In four cases of the thirty-seven no operation had been performed, and the cases were still in the operable stage. In one of the four, however, complications contraindicated operation. Of the remaining thirty-three, six had not been operated upon, but were inoperable when the enzyme treatment was begun. The other cases (twenty-seven) were inoperable ones, in many of which exploratory or palliative operations had been performed. Ten cases (Nos. 33, 79, 86, 87, 89, 90, 91, 93, 95 and 98) were followed throughout the entire course of their treatment by the enzyme method.

In ten cases of the thirty-seven there was an anemia of the chlorotic type. In eight of these it developed only in the last stages of the disease. The other cases showed a mild varying grade of secondary anemia. Nucleated reds, of the type of normoblasts, were rather rare. The hemoglobin in the more severe cases varied between 45 and 75 per cent.; the number of reds from 2,168,000 to 5,580,000 per cubic millimeter. In no test was the hemoglobin ever higher than 85 per cent. (Fleischl hemoglobinometer).

In five cases there was an improvement in the hemoglobin during the first few weeks of enzyme treatment. In Case No. 32 there was an increase from 80 to 85 per cent., and a gain of 100,000 red blood corpuscles. The hemoglobin subsequently dropped to 70 per cent., the red cells remaining about the same. In Case No. 50 there was likewise an improvement of about 5 per cent. hemoglobin during the first two months of treatment. In Case No. 44 there was a gain of 12 per cent. hemoglobin and of nearly 700,000 red cells per cubic centimeter during four weeks of treatment. In this case the treatment was begun very soon after an operation and the gain can therefore be ascribed in but small part, if at all, to the treatment. In Case No. 79 there was an improvement of about 4 per cent., which was subsequently lost. This gain was also post-operative. In Case No. 98 there was an increase of about 5 per cent., hemoglobin and an increase of 200,000 reds per cubic centimeter during the first four weeks the patient was in the hospital.

Leucocyte and differential counts were made in four enzyme cases and one control case (Nos. 79, 91, 92, 95 and 98) three times, at the same hour on three different days, before beginning the injections. In ten enzyme cases (Nos. 22, 33, 35, 36, 44, 49, 80, 86, 87, 89, 91 and 93) and two control cases (Nos. 35 and 91) leucocyte and differential

counts were made once before the beginning of the treatment. In the remaining ten cases the blood examinations were begun after the patients had had the treatment for from one to thirty weeks. In a few cases which were carefully observed during the first week or two weeks of injections there was a gradual and moderate increase in the total number of leucocytes; however, in only two cases could there be said to be no other causative factor than the trypsin injections. In five cases of cancer of the breast there was no total leucocyte count over 12,500 per cubic millimeter which could not be ascribed to causes other than the cancer. In five cases of epithelioma there was no total leucocyte count over 9,500 per cubic millimeter not accountable for by necrosis, ulceration or other complication. The counts on the cases in which there was marked ulceration and sloughing varied between 23,500 and 34,000 per cubic millimeter.

Blood smears were made in the mornings between one and one-and-a-half hours before the noon meal and at a corresponding hour in the individual cases. Cases from the Dispensary came at corresponding hours between two and three P. M. The Wright stain was used as a rule, in some instances Ehrlich's triple stain. In making the differential counts 500 cells were counted, in some instances 1,000 cells, and in three instances only 300 or 400 cells. Over 300 differential counts were made.

The following classification was followed: polymorphonuclear neutrophiles, large mononuclears and transitionals, small mononuclears (size under polymorphonuclear), eosinophiles, mast cells, and myelocytes. Under the head of small mononuclears were included the non-granular mononuclear cells with central nucleus and small amount of protoplasm, and the mononuclear cells with small eccentric nucleus and non-granular protoplasm, present in larger amount than in the above. The size of these cells so counted was under that of the polymorphonuclear cells. For purposes of charting, the percentages of large mononuclears and transitionals were averaged together.

SUMMARY OF BLOOD EXAMINATIONS.

A relative lymphocytosis was found at some time in the course of thirteen cases out of twenty here described. In two other cases observed over a period of three months, in which counts were not quite so frequently made and not given here, there was also a relative lymphocytosis found, making the number of cases fifteen out of twenty-two. The relative lymphocytosis was present sometimes before the beginning of the trypsin treatment, while injections were being given, and after treatment was discontinued. It was found at times in the control cases. When the course of the disease was apparently held in check the lymphocytes were relatively normal, below, or very slightly increased. In those cases in which the disease was steadily progressing the small mononuclears reached the highest relative per cent., dependent in a measure, however, on the presence or absence of complications. In the presence of any complication causing high increase in the polymorphonuclear neutrophiles the small mononuclears were, as a rule, relatively low. Out of the fifteen cases above mentioned (four epitheliomata and eleven carcinomata), nine cancers were in such locality that extension by the lymphatics and glands would naturally follow. Four were pelvic and abdominal cases of cancer, in which any progressive glandular involvement was not demonstrable. One was a case of epithelioma of the lower jaw, in which the relative per cent. was quite high, but glandular involvement was not certain. In the other seven cases of the twenty-two, in all except one there was a complication present, causing a relative and absolute increase in the polymorphonuclear

cells. This one case was observed only over a period of four weeks following operation.

It is desired to emphasize the presence of a relative lymphocytosis (increase of small mononuclears) found present in the course of the above cases (irrespective of treatment) in association with progressive growth of the cancer or metastatic formation, and, frequently, found present before increased growth or enlarged or new metastases were clinically demonstrable. With the exception of four cases out of the twenty that were observed over a period of from 6 weeks to 7 months, the eosinophile cells showed a steady increase in numbers while the patients were upon the trypsin injections. Upon discontinuing the injections the eosinophile cells dropped in numbers, reaching the normal average, or much below it, in about two weeks' time. This fall in numbers per cubic millimeter occurred in every instance, although the internal treatment was continued regularly. If, because of refusal on the part of the patient or because of the general condition of the patient, two or three treatments were skipped, it was apparent in the temporary decrease in the total number of eosinophiles. In no case, however, was the relative per cent. greater than twelve, although the trypsin injections were in many of the cases pushed to the limit for the individual in question. There was no eosinophilia in any of the control cases except where there was involvement of bone.

The exact etiology of this eosinophilia is speculative. One cause which is suggested is the absorption or attempted absorption of the trypsin from the subcutaneous tissues. The eosinophilia does not entirely disappear when the patient is put on amylopsin injections after discontinuing the trypsin. This is so judged as the count falls still lower after discontinuing all injections. There were no nodules as the result of amylopsin injections. Incidentally it may be remarked that injections of amylopsin into trypsin nodules did not in any degree hasten their absorption. In cases on the internal treatment alone there was no eosinophilia observed, although it is claimed (von Leyden and Bergell) that trypsin passes into the general circulation from internal administration and may be absorbed in large amounts. In four of the cases in which there was rectal or other intestinal involvement eosinophiles were present before treatment in from three to five per cent., representing 300 to 700 per cubic millimeter. In three cases with bone involvement (not on trypsin) eosinophiles were present in from four to six per cent., representing 460 to 1,080 eosinophiles per cubic millimeter.

URINE.

In an attempt to ascertain if there was any irritating action exerted by the trypsin on the kidneys in the cases in which it was given by mouth, hypodermatically, or by other methods, ordinary urine tests were made in connection with twenty-three cases treated with trypsin. In eight cases uranalyses were made before treatment was instituted, then every day for the first week or ten days of treatment, and thereafter as was deemed advisable. In five out of this eight neither casts nor albumin were present at any time in the urine. In two out of the eight cases there was an occasional trace of albumin, hyaline and sometimes few granular casts in the urine before the injections were begun. This condition varied while the patients were on the treatment. In one instance there was a slight exacerbation in the kidney lesion following constant and rather large doses of the trypsin. In the remaining case out of the eight, the treatment was given for a week and then discontinued for a second operation, the removal of a recurrent nodule. Following this operation the patient had a slight cold, and when the uranalyses were resumed in connection with the trypsin

injections, there was a small amount of albumin, finely granular and few hyaline casts present in the urine. The patient left the hospital soon after this, and while the treatment was continued for some time no uranalyses were made outside of the hospital. In this instance casts and albumin were not present before treatment or before the second operation.

In the urine of a few cases out of the other fifteen, of the twenty-three, granular, hyaline, and few pus casts, and occasionally albumin, were observed in the very last stages of the disease. With one exception they were not present at other times. In this case, an old man over ninety, with epithelioma of the ear, there were constantly present the evidences of nephritis. The treatment had been given in large doses from the beginning, and the patient had had an acute exacerbation of the nephritis. Upon resuming the trypsin injections a second time, small increasing doses were used; it was this time taken for eight weeks, when symptoms of a beginning exacerbation of the nephritis became evident.

It was desired to study the excretion of the chlorides, phosphates, and sulphates in connection with the trypsin treatment, but owing to the difficulty of securing a sufficient number of uncomplicated cancer cases from whom twenty-four hour specimens of urine could be regularly obtained this was not done.

The following method was used in testing the urine for an enzyme with properties of digestion similar to trypsin (see Hedin; *Jour. of Phys.*, Vol. XXX, 1903, pp. 155–195; also Cathcart; Products of Urotryptic Digestion, Salkowski's Festschrift, 1904.) For the following work urine with a specific gravity of 1011 and under was used undiluted, while urine with a specific gravity over 1011 was diluted one-third or one-half with distilled water. To each 1000 c.c. of the urine or urine mixture was added 5 c.c. of a $3\frac{1}{2}$ per cent. solution of casein in 0.25 per cent. sodium carbonate. To less amounts, 750 or 500 c.c., was added 3 or $2\frac{1}{2}$ c.c. of the $3\frac{1}{2}$ per cent. solution of casein. The casein after thorough mixing with the urine was precipitated by 20 per cent. acetic acid. After complete precipitation the supernatant fluid was siphoned off and the precipitate transferred to a filter and washed free of acid with distilled water. After thorough washing the casein-enzyme combination was transferred in each case to a six ounce sterile glass-stoppered bottle, which was then filled with 0.25 per cent. or 0.5 per cent. solution of sodium carbonate made with distilled water. To each bottle were added a few pieces of fibrin that had been boiled for fifteen minutes. Toluol and choloform were then added to each bottle to prevent putrefaction. The various bottles, labeled with date and name of patient, were kept in the thermostat for from one to seven months at a temperature ranging between 35 deg. and 37 deg. C.

Four cancer cases on the trypsin treatment and a control case (epileptic) were selected as suitable, and three times a week twenty-four-hour specimens of urine were heated and the casein separated out as above described. The casein combination in each case was transferred after thorough washing to a sterile six ounce bottle, filled with 0.25 per cent. sodium carbonate, and a small amount of *unboiled* fibrin added. Toluol and chloroform were added and the bottles placed in the thermostat as soon as they were finished. These digests were made over a period of three weeks. Upon examination daily there was evident a gradual dissolving of the fibrin, and at the end of six weeks the amino-acids were found present in each case. These findings led to the making of some control digests.

Two sterile six-ounce bottles were filled with 0.25 per cent. sodium carbonate made with distilled water, and to each one was added $2\frac{1}{2}$ cubic centimeters of a $3\frac{1}{2}$ per cent. solution of casein. Two other sterile bottles were filled with a 0.25 per cent. sodium carbonate, and $2\frac{1}{2}$ cubic centimeters of a $3\frac{1}{2}$ per cent. solution of casein, and

a few pieces of unboiled fibrin were added to each bottle. To another series of two bottles which were filled with 0.25 per cent. sodium carbonate were added 2½ cubic centimeters of 3½ per cent. casein solution, and a few flakes of fibrin that had been boiled for fifteen minutes. To each of the above bottles were added toluol and chloroform and they were placed in the thermostat. Observed over a period of six weeks numbers I and II of the first series remained perfectly clear, a few grains of casein being demonstrable at the bottom of the bottles. Numbers I and II of the second series showed solution of the fibrin. Number I of the third series showed slight solution of the fibrin (boiled); number II of the third series showed no change in the fibrin. Upon examination for digest products (about six weeks' time) the casein was found unaltered in bottles I and II of the first series. In the second series to which unboiled fibrin had been added digestion products were demonstrable in both bottles. In number I of the third series there was some digestion; this bottle had been frequently opened and contained *very small* amounts of the preservatives. That the bottle became contaminated was evidenced later by its odor. Bottle number II of the third series showed no digestion.

Two more digests according to series III were made about one month later than the above. In this series number IV there was no digestion. During this month and the following there were many digests made from specimens of urine from different trypsin cases and control cases, to which the boiled fibrin was added; but not until March, 1908, was there a definite series of cases followed every day for a couple of weeks.

In March two cases on the regular trypsin treatment were selected, one a case of abdominal carcinoma, the other a case of carcinoma of the base of the tongue, epiglottis and glands of the neck. Two control cases were selected, one a patient not having cancer, the other a cancer case, but not on the trypsin treatment. Twenty-four-hour specimens of urine (when possible) or single specimens were obtained from these four patients twelve out of seventeen consecutive days. The method above described was used in separating out the supposed casein-enzyme and preparing it in each instance for the thermostat. Boiled fibrin was used in the thirty-four digests made. These digests were all kept in the brood oven four months; twelve of them were afterward kept at room temperature for another three months. In eight instances out of the thirty-four there was no evidence of any digestion of the fibrin. In three more cases there was some dissolving of the fibrin, but the presence of any of the group of amino-acids could not be demonstrated. Thus there were eleven negative digests in the thirty-four. In one control case (not cancer) the results were negative five times out of seven, but positive in the other two cases. In the other control case two digests were negative. In the trypsin cases results were negative in one instance twice and in the other three times. In seven of these eleven negative digests the urines when treated were slightly alkaline from beginning ammoniacal decomposition. These urines were probably neutral or slightly alkaline when voided. In the four other negative instances all digests made on the two days these were made gave negative results. It is possible that the casein was not sufficiently well mixed with the urines to separate any enzyme present.

In the other twenty-three digests the amino-acid group was found present in each one.

The above experiments showed the presence in the urine in cases on the trypsin treatment, in noncancerous patients, and in patients with cancer who had not been treated by trypsin, of an enzyme possessing properties of digestion similar to trypsin. This body was not found in urines in which there was beginning ammoniacal decomposition. No attempt was made to ascertain the appearance or disappearance of the

body in the urine during the various stages of a cancer case, which might be of interest in connection with the known anti-tryptic action of the serum in all cases of severe anemia, and said by Brieger and Trebing (*Berliner klin. Woch.*, July 20, 1908) to be present early in all cancer cases, and to be influenced by the administration of pancreatin as shown by a remarkable fall in this antitryptic action of the serum.

EFFECT OF TRYPSIN UPON THE TISSUES.

In submitting sections to pathologists for examination, in all cases where the tissues were removed after the institution of the enzyme treatment, it was requested that especial attention be directed to the determination of any structural changes that might in any way be attributable to the action of trypsin. Whenever it was possible to do so specimens were taken from time to time, care being taken in every instance not to encroach upon nature's barriers. Comparative studies were thus made of the pathological tissues before beginning the enzyme treatment, at various times during its course, and in some instances after the death of the patient.

Dr. F. B. Mallory, Professor of Pathology, Harvard Medical School, who made a number of examinations, found nothing that he could in any wise attribute to the action of the trypsin.

Dr. Martha Wollstein, Pathologist to the New York Skin and Cancer Hospital, who made the largest number of examinations during the course of the test, found no tissue changes which could be ascribed to the action of the trypsin.

Dr. James Ewing, Professor of Pathology, Cornell University Medical Department, after careful study of the specimens submitted to him, made the following statement: "In several sections the central cells in many tumor masses were loosened, degenerating or necrotic, while only the outer layers of cells adherent to an infiltrated lymph space seemed to retain their vitality. In some cases of cancerous infiltration of the uterine muscle originally larger tumor cell masses appeared to have been reduced by this process to thin strands of degenerating epithelial cells, and in some rather wide areas the tumor infiltration took the form of isolated cells scattered at wide intervals. In some cases a peculiar edema and vacuolar degeneration was prominent. but this condition differed only in degree from that sometimes seen in untreated cases.

"Occasionally there was encountered a peculiar edema and granular degeneration and fragmentation of fibrous, connective, and smooth muscle tissues which I have not seen in untreated cases. In all the cases considerable portions of the growth appeared little or not at all affected by the above mentioned degenerative processes, a fact which may account for the steady clinical progress of the disease. In one or two cases there appeared to be no change whatever referable to the treatment."

CASE REPORTS.

In the cases which follow only such details are given as have a bearing upon the blood examinations. For all other data the reader is referred to the accompanying table, in which we have endeavored to give the essential facts concerning each case.

Case 33.—Carcinoma of Uterus and Abdominal Viscera. Patient was first given glycerin and sterile water injections for nine days, with no subjective or objective results. She was then given alternate injections of trypsin and amylopsin from December 21, 1907, to January 24, 1908, and from that time irregularly to February 20. Ten days after beginning the regular emzyme treatment the blood showed hemoglobin 60 per cent., few normoblasts, microcytes and pale red cells. Total white blood count 22,000. This ranged between 22,000 and 29,500 per cubic

millimeter. Polymorphonuclear cells relatively and absolutely much increased, numbering 25,549 per cubic millimeter two weeks before death. There was a relative decrease in small mononuclears, the total number, however, varying from normal to 1,800 per cubic millimeter above normal. The eosinophiles steadily increased from 468 to 1408 per cubic millimeter one week before death. Hemoglobin at this stage 51 per cent. The rapid decline of the patient during the course of the treatment was doubtless due to the advanced stage of the disease rather than to the treatment.

Case 50.—Carcinoma of Breast; Operable; Operation Refused. Trypsin and amylopsin given alternately from December 7, 1907, to January 6, 1908. On account of an attack of acute influenza, with coincidental abscess formation at the site of one of the injections, treatment was suspended until February 11, 1908, when it was resumed and continued until February 26. Internal treatment with Holadin and ox-gall given continuously from December 7 to February 26. While on the treatment the total white cell count varied between 6,500 and 10,500 per cubic millimeter. The small and large mononuclears fluctuated relatively above normal. The eosinophiles, which were 78 per cubic millimeter in a count made before beginning the treatment, were 940 per cubic millimeter the day of discharge from the hospital.

Case 51. Ephithelioma of Auricle; Inoperable. Nine injections of trypsin were given between February 8 and 29, 1908. Trypsin was then discontinued because of an acute exacerbation of an old kidney lesion. Amylopsin was given until March 13, when trypsin was resumed. Thirty-one injections of trypsin were given between March 14 and May 12, 1908. Treatment was then discontinued, as the disease was slowly progressing, and the patient complained bitterly of the painful injections. The total white cell count varied between 8,500 and 11,500 per cubic millimeter while the trypsin injections were being given. The small mononuclears were relatively below normal from March 14 to April 7; from April 9 they fluctuated above normal; from April 27, from 7 to 12 per cent. above. On June 2 there was a moderate absolute as well as relative lymphocytosis present. From this time until the discontinuance of the blood counts July 15, two months after the injections ceased, there was a relative lymphocytosis of one per cent. At the beginning of the treatment the large mononuclears and transitionals were relatively high. The eosinophiles gradually increased from 198 on March 24, to 920 on April 28, 1908; from May 5 to May 12 there was an increase from 665 to 1012, and in the two weeks following they decreased to 331.

Case 78.—Recurrent Carcinoma of the Left Breast, and Supraclavicular and Infraclavicular Glands, following amputation. Regular enzyme treatment instituted July 1, 1907, and continued until April 4, 1908. During this time the patient received 70 injections of trypsin and 40 of amylopsin. The internal treatment was given throughout the entire time the patient was under observation. Three abscesses formed at the sites of injections, apparently from nonabsorption of the material. During April and May there was a gradual increase in the size of the left arm, which slowly decreased during June.

In September, at the patient's request, the trypsin injections were again instituted. Twelve injections of trypsin and four of amylopsin were given during the second course of treatment. At the time of beginning the blood examinations in April, 1908, the patient had been on amylopsin for over a month. During April there was a relative lymphocytosis (increase of small mononuclears) of 9 to 20 per cent. above the normal average, the total number of small mononuclears varying between 3,420 and 6,195 per cubic millimeter. This was in the month preceding the marked evidences of renewed growth objectively present in May. The relative increase of these small mononuclears in May was 8 to 11 per cent. above the normal average. From July 15

to September 1, but one blood count was made. During the second return to trypsin injections the percentage of small mononuclears was not relatively increased as constantly or as high as in the preceding months, the total numbers averaging between 1,160 and 3,325 per cubic millimeter. The eosinophiles during April and May varied between 155 and 245 per cubic millimeter; after discontinuing all injections between 85 and 113 per cubic millimeter, during September and October they increased to 300 per cubic millimeter.

Case 80.—Carcinoma of Uterus and Bladder (irremovable), with presence of vesico-vaginal fistula for three weeks. Trypsin was begun May 6 and continued until May 20. May 21 curettage and cauterization were performed. Patient left the hospital June 3, reporting thereafter at the dispensary for the trypsin treatments which were continued until November 2, 1908. Five injections of amylopsin were given, making fifty-five injections in all. Holadin, begun May 6, was continued regularly during the treatment. There was a hyperleucocytosis during the first week in May, but this was within three weeks of the operation. While on the treatment from June 3 to July 22, the counts were practically normal. During this time there was a slight gain in weight and some improvement in the secondary anemia present. There was also less passage of urine through the vesico-vaginal fistula. From July 22 on there was a total white cell count varying between 14,000 and 18,000. From the first of August there was a leucorrhea present and the patient suffered occasionally from slight hemorrhages from the uterus. All the white blood cells were increased, the percentages remaining nearly normal, with the exception of the eosinophiles, until the latter part of September. From then on a slight relative lymphocytosis was present except when masked by the polymorphonuclear cells. The red blood cells, October 22, numbered 2,268,000 per cubic millimeter, the hemoglobin was 70 per cent. An occasional normoblast was present. The eosinophiles increased, with slight fluctuations depending apparently upon whether a treatment or two was skipped, from 370 per cubic millimeter to 1,484 per cubic millimeter.

Case 88.—Operable Carcinoma of Breast; Operation refused. Regular enzyme treatment from June to November, 1908. Forty-seven injections given. From June until July 29 there was a relative lymphocytosis present. During August but seven treatments were given as nodules formed at the site of the injections, which became inflamed. During September but four treatments were given because of the formation of two abscesses that had to be lanced. During these two months there was a relative if not absolute increase in the polymorphonuclear cells. The injections were begun regularly again towards the last of September and continued until the first of November. There was an increasing relative lymphocytosis from September 22. The eosinophiles varied from 1 to 3 per cent. and again from 1 to 4.2 per cent. during the first and second regular courses of treatment. November 1 the patient's general condition seemed about the same save for slight loss in weight. The anemia had not improved.

Case 91.—Inoperable Cancer of Abdominal Viscera. Control case. Patient cachectic, weak, and losing weight. From January 13 to March 15, 1908, injections of sterile water were given, with negative subjective and objective results. March 15, with a white cell count of 22,500, of which 12,510 were polymorphonuclear cells, 4,216 small mononuclears, and 415 eosinophiles per cubic millimeter, the injections were changed to amylopsin every other day, the object being to observe the eliminative action. These injections were given irregularly from March 15 to April 11, 1908, during which time there was a continued increase of from 4 to 9 per cent. of small mononuclears and a relative decrease of polynuclears from 10 to 14 per cent., with a

white cell count varying between 15,000 and 17,000 per cubic millimeter. The full enzyme treatment was given from April 11 to May 1, 1908. During April the progressive loss of weight was apparently slightly checked. On May 9 the sterile water injections were resumed. The last of May the patient developed a recto-vaginal fistula which caused her confinement to bed. She gradually became more cachectic and thinner until death in July.

During March and April there was a varying lymphocytosis of from 4 to 11 per cent. From the last of May to the middle of June there was a relative increase in the polymorphonuclear cells. From the middle of June on there was a relative increase in the small mononuclears, the total count of June 29 showing 48 per cent. From that time on there was a relative increase in the polymorphonuclear cells, with a relative decrease of small mononuclears until death. June 29 was the only instance in which the polynuclears were found present in numbers less than 7,000 per cubic millimeter. With the relative increase of small mononuclears during June there was also a relative increase in the large mononuclears and transitionals to 14 per cent. Eosinophiles varied between 2 per cent. and 5.6 per cent; lymphocytes averaged between 2,044 and 9,900 per cubic millimeter.

Case 92.—Epithelioma of Chin and Lower Jaw. Control case. Sterile water injections were begun the last of May, shortly after the second operation. The blood counts showed a marked relative lymphocytosis, there being from 44 to 49 per cent. of small mononuclears in a total white cell count varying between 7,500 and 8,500. June 11 they dropped to 24 per cent., rising relatively to 48 per cent. on June 16, two days before the patient's third operation. The eosinophiles increased from 37 per cubic millimeter June 4 to 552 per cubic millimeter June 16—to be expected from involvement of bone. A white cell count was not again made until July 25, when there was a relative lymphocytosis of 35.8 per cent. of large mononuclears and transitionals out of a total count of 6,000 white blood cells per cubic millimeter. The increase of small and large mononuclears continued until the fourth operation, August 25, 1908. Two weeks later the counts were relatively 26.2 per cent. and 8.8 per cent., the polynuclears being 63.8 per cent. September 23 the small mononuclears were again relatively high, 43.8 per cent., while the large mononuclears were nearer normal, 7.8 per cent. The small mononuclears varied the following five weeks between 38 per cent. and 43.4 per cent. During these five weeks the total white cell count varied between 9,500 and 11,000 per cubic millimeter. The eosinophiles increased from 105 to 315 per cubic millimeter. Injections of sterile water were now discontinued; the internal administration of holadin was also stopped. The patient began to gain in weight at the rate of a pound and three-quarters a week. The hemoglobin improved slightly and the number of red cells increased.

Case 94.—Carcinoma of Uterus, Tubes, Ovaries and Broad Ligaments, recurrent after operation for carcinoma of rectum. Uterine and ovarian arteries ligated, February 7, 1908. Full enzyme treatment begun February 24. During March the injections were taken regularly, irregularly during May, still more so during June, and discontinued entirely July 18. Patient failed rapidly. The first blood count that showed any relative increase in the small mononuclears was April 22, when they formed 27.2 per cent. of a total white blood cell count of 15,000 per cubic millimeter. During May there was a relative increase of small mononuclears of from 6 to 11 per cent., which continued until the middle of June. From then on there was an increasing relative and absolute leucocytosis, and a slowly progressive anemia. About the middle of June the patient suffered from severe pain in the rectum, examination revealing new recurrences. Pain from this time on was so constant and severe that large doses of

morphine were necessary. On July 31 a recto-vaginal fistula developed. Holadin was stopped July 31; two days later the patient suffered from severe abdominal distension with gas. This distension continued to a greater or less degree until death, August 17. The eosinophile count varied from 3.4 per cent. before the beginning of treatment to 2 per cent., dropping to 0.8 per cent. in July, when the total white cell counts were high. A few myelocytes were present in the blood in July. There were no nucleated reds found at any time.

WORK OF OTHERS

In order to ascertain the experience of others with the method, as Secretary of the Committee on Scientific Research of the New York Skin and Cancer Hospital, the writer sent letters of inquiry to more than three thousand representative physicians and surgeons, a large proportion of whom had been furnished material by Mr. Fairchild, and were known, therefore, to have employed the treatment.

The following questions were asked:

(1) Have you employed this method? (2) In how many cases? (3) Diagnosis of each: (a) Clinical, (b) Microscopic. (4) How employed? (5) Results. (6) Conclusions. Seven hundred and eighty replies were received. Of this number 304 reported no experience. Those having had experience reported a total of 949 cases treated. Of this number of cases 248 were given as favorably influenced as to pain, local or general condition, but not as to the ultimate outcome of the disease. With the exception of thirteen cases, the remainder were reported as doubtful or negative. In this summary I have excluded a consideration of reports which were clearly fictitious, for example, as, when a physician makes the sweeping statement that he has employed the method in over a hundred cases, all of which were cured. It may be said in passing that the thirteen alleged cures do not embrace the celebrated "Case I" and others of Morton's published report. Of the thirteen cures four had only the clinical diagnosis, and the evidence in support of malignancy was insufficient. In one of these cases the physician who reported it expressed doubt as to the correctness of the diagnosis. In the other nine of the thirteen cures, some of which were still under treatment when the report was made, the end result is not known, but, reasoning from analogy, it is quite probable that these, like the celebrated Case No. I of Dr. Morton's series, have made their exitus while being published as cured.*

It is interesting to note, in connection with these supposed cures, that those stated most positively as cured up to the time of report were diagnosed as cancer of the stomach. How much of the improvement in any of the cases is attributable to the regime is a question. The fact that our control cases did as well with injections of glycerin and sterile water or sterile water alone, plus the regime, as did the others with the full enzyme treatment leads to the belief that the regime plays a most conspicuous part in the production of whatever favorable results were noted.

Reports of the experiments with the enzyme treatment which have been made at the Middlesex Hospital, and by Shaw, Mackenzie, von Leyden, and a number of European authorities, have appeared in the medical press from time to time, and are not included in the above summary.

*Should any reader of this report have further data along this line, the Committee on Scientific Research would be glad to receive such information.

Case	Name	Sex	Age	Nationality	Color	Single Married	Occupation	Private or Hospital	Referred by or in Consultation with	Diagnosis: 1 Clinical 2 Microscopic	Location of Disease	Durat Dise Previo Enz Treat
1	L. H. B..	M..	38	U. S.....	White.	Married	Salesman..	Private..	.....	1 Carcinoma 2 Squamous-celled carcinoma.	Primary: Tongue and glands of neck. Secondary: Floor of mouth and neck.	1½ yea
2	M. R....	M..	39	German-American	White.	Married	Cab driver.	Hospital	Wm. T. Bull, N. Y. City.	1 Carcinoma 2 Carcinoma	Tongue and glands of neck.	1½ yea
3	B. V....	M..	68	German....	White.	Married	Tailor.....	Hospital.	Fred Wise, N. Y. City.	1 Carcinoma 2 Carcinoma	Bladder and prostate....	9 mont
4	I. L.....	F..	38	U. S.....	White.	Married	Housewife.	Hospital.	.....	1 Carcinoma 2 Carcinoma	Right breast.....	1 year.
5	T. E. W.	F..	44	U. S.....	White.	Married	Housewife.	Private..	.....	1 Carcinoma. 2 Carcinoma.	Primary: Uterus..... Secondary: Abdominal viscera.	15 mo
6	E. M. P..	F..	56	U. S.....	White.	Married	Housewife.	Private..	J. Walker, Brooklyn, N. Y.	1 Carcinoma. 2 Carcinoma.	Uterus, part of vaginal wall and bladder.	About
7	K. H....	F..	49.	U. S.....	White.	Single..	.....	Private..	Edward W. Peet, N. Y City.	1 Carcinoma. 2 Carcinoma.	Primary: Left breast.... Secondary: Contiguous skin, axillary glands, chest wall, neck, pleura, lungs, abdominal organs	About
8	W. K....	F..	72	U. S.....	White.	Married	Housewife.	Private..	L. Nevin, Jersey City, N. J.	1 Carcinoma. 2 Carcinoma.	Uterus, broad ligaments and bladder.	About
9	C. J. W..	F..	51	U. S.....	White.	Married	Housewife.	Private..	E. O. Palmer, Hollywood, Cal.	1 Carcinoma. 2 Carcinoma.	Primary: Left breast.... Secondary: Skin over primary seat; glands of neck and axilla; probably liver.	15 mo
10	J. L. S...	F..	51	U. S.....	White.	Married	Housewife.	Private..	J. H. Jenkin, Shrub Oak, N.Y	1 Carcinoma. 2 Carcinoma.	Body of uterus, broad ligaments, glands of pelvis.	2½ mo
11	M. J. B..	M..	70	U. S.....	White.	Married	.....	Private..	A. V. Rockwell, N. Y. City.	1 Carcinoma.	Stomach.....	6 mont
12	M. A. S..	F..	78	U. S.....	White.	Single..	Teacher....	Private..	F. S. Emerson, Brooklyn, N.Y.	1 Carcinoma. 2 Carcinoma of scirrhus type.	Right breast, glands of neck and axilla.	9 yrs. tum brea yrs a growt
13	J. I.....	M..	37	U. S.....	White.	Married	Mason.....	Hospital.	E. F. Gissler, Brooklyn, N. Y.	1 Carcinoma. 2 Carcinoma.	Primary: Lower lip..... Secondary: Lower lip, lower jaw, glands of neck.	2½ yea
14	S. G.....	M..	35	Russia.....	White.	Married	Tailor.....	Hospital.	Max Einhorn, N. Y. City. Henry Franciscus, Brooklyn, N. Y.	1 Carcinoma.	Lower part of esophagus and stomach.	9 mont
15	J. V.....	M..	44	German....	White.	Married	.....	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Primary: Lower lip..... Secondary: Lower lip, glands of neck.	8 mont
16	J. K.....	M..	43	Bohemian..	White.	Married	Bricklayer.	Hospital.	.....	1 Carcinoma. 2 Squamous-celled epithelioma.	Penis and inguinal glands	6 mont

Previous Treatment	Condition When Enzyme Treatment Was Begun	Duration of Enzyme Treatment	Effect Upon: 1 Local Condition; 2 General Condition; 3 Fetor; 4 Pain; 5 Progress of the Disease.	Result
philitic for 1 year (other physic- Removal of glands of neck, Mar. 07; removal of left half and part of half of floor of mouth and left of tongue, Mar. 27, 1907 (Bain- e).	Recurrence in floor of mouth and neck. Inoperable.	June 1, to July 12, 1907. Large doses, full regime.	1 Hastened breaking down of tissue; assisted in cleansing. 2 None. 3 Slightly lessened. 4 None. 5 None.	Died Sept. 15, 1907.
perations for removal of glands ck and part of tongue (Dr. W. T.	Recurrence in tissues of neck. Inoperable.	Apr. 25 to June 29, 1907. Large doses, full regime.	1 Wound became cleaner and diminished in size by one-third during early part of treatment. 2 None. 3 Lessened. 4 None. 5 None.	Died July 10,1907.
al medication and *x*-ray (another tal). Refused operation for three hs while on enzyme treatment, suprapubic cystotomy (another tal). Leucodescent light concur- with enzyme treatment.	Hematuria. Pain in region of bladder and prostate, very severe on urination; emaciated, weak.	Feb. 27 to June 2, 1907. Large doses caused chills.	Negative in all respects.	Died June 12, 1907.
ete amputation of breast (another tal).	Recurrence in scar; ulceration. Refused further operation.	May 2 to July 15, 1907.	1 None. 2 Temporary marked improvement. 3 None. 4 None. 5 None.	Died Feb. 15,1908.
ectomy (Bainbridge), June 29,	Recurrence in abdominal viscera. Constant pain; hemorrhage from rectum.	Apr. 23 to June 12, 1907. Large doses, full regime.	1 Temporary apparent improvement. 2 Gained in weight at first; temporary general improvement. 3 Lessened. 4 Lessened at first. 5 None.	Died June 18, 1907.
n powder locally, 1 mo.; curett- trypsin and amylopsin in very doses irregularly for 8 weeks; ylene blue for 2 mo. (other cians.)	Inoperable. Suffering from toxemia due to absorption of cancerous products. General condition very poor.	Dec. 11, 1906, to May 17, 1907. Full treatment.	Temporary improvement in both local and general condition, followed by rapid decline. Tendency to non-absorption of large doses of trypsin, resulting in a few so-called abscesses, which necessitated discontinuance of treatment for a few days at the time.	Died May 19,1907
al of growth from left breast, 4, 1904 (Dr. Edward W. Peet), l operation refused. About 1 later, 32 *x*-ray treatments (Dr. J. Morton); trypsin, 5 to 10 minim Apr. 27 to Oct. 31, 1906 (Dr. n). Radical operation, Nov. 3, (Bainbridge). Removal of en- l nodules and secondary deposits n, Jan. 22, 1907 (Bainbridge).	Full enzyme treatment instituted twenty-four days after radical operation. Recurrent; irremovable cancer of left side of chest and glands of neck; liver enlarged probably cancerous; general condition poor.	Nov. 27, 1906 to Mar. 20, 1907. Full regime, with increasing doses of trypsin and amylopsin.	1 Ulcerated surfaces cleared up by lotio pancreatis. 2 None. 3 None. 4 None. 5 Did not prevent recurrence or otherwise influence the disease.	Died Mar. 23, 1907.
age; small doses trypsin for 20 (Nevin).	Irremovable cancer of uterus, broad ligaments and bladder.	Feb. 2 to Mar. 23, 1907.	1 Temporary apparent improvement. 2 Temporary apparent improvement. 3 Lessened at first. 4 Lessened at first. 5 None.	Died Mar. 25, 1907.
al of primary growth in breast, 2, 1906 (another surgeon). Re- l of glands of neck and axilla, 1, 1907 (Bainbridge).	Enzyme treatment begun immediately after removal of glands of neck and axilla. Liver enlarged, probably cancerous. General condition very poor.	Jan. 24 to Apr. 14, 1907.	Negative in all respects.	Died Sept. 1, 1907.
r" cancer treatment 4 weeks. es.	Irremovable cancer.....	Apr. 14 to May 15, 1907	Negative in all respects.	Died May 26,1907.
l treatment.....	Usual symptoms of cancer of stomach.	Apr. 8 to 15, 1907.....	Negative in all respects.	Died Apr. 20,1907.
ve. Refused operation for 15 mo. active growth of disease. Re- of breast and enlarged glands, 7, 1907 (Bainbridge).	Operable cancer of right breast, with area of ulceration about size of fifty-cent piece. Glands in neck and axilla enlarged.	Dec. 19, 1906 to Jan. 22, 1907. Returned home, treatment continued for 3 months.	1 Ulcerating surface cleaned. 2 Temporary slight improvement. 3 No fetor present. 4 No pain. 5 None.	Died May 17,1908.
cauterization; removal of growth "Curry treatment" (other phys- . Trypsin, 10 minims every other une 15 to July 15, 1907 (other ian).	Large, discharging mass involving entire lower jaw and glands of neck.	July 15 to Sept. 1,1907. Full treatment.	Negative in all respects.	Died Sept. 20, 1907.
n for 3 weeks (another physician).	Emaciated; great pain; dysphagia. Operation refused.	Mar. 24 to June 21, 1907.	Temporary improvement in general condition; dysphagia less marked. Later grew rapidly worse.	Died Sept. 15, 1907.
y growth removed, Apr. 15, 1907 er physician); secondary growth ced for 2 months (another ian).	Inoperable recurrent carcinoma of lip and glands of neck; mass in neck broken down and discharging freely.	June 22 to Aug. 12, 1907.	1 Hastened breaking down of mass in neck. 2 Temporary improvement. 3 None. 4 None. 5 None.	Died Sept. 7, 1907.
l medication and ointments loc- other physicians). Removal of guinal glands and high amputa- f penis, Dec. 10, 1906 (Bain-).	Enzyme treatment begun immediately after operation.	Dec. 11, 1906 to Apr. 28, 1907. (100 minims of "Quadruple X" trypsin, alternating with amylopsin of same strength.)	Temporary gain in weight and improvement of general condition. Otherwise negative.	Died June 9, 1907

Case	Name	Sex	Age	Nationality	Color	Single Married	Occupation	Private or Hospital	Referred by or in Consultation with	Diagnosis: 1 Clinical 2 Microscopic	Location of Disease	Duratio Disea Previou Enzy Treatn
17	F. S.....	F..	38	U. S.....	Color'd	Married	Housewife.	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Uterus.....	5 month
18	M. D....	M..	57	Irish.....	White.	Married	Watchman	Private..	E. A. Miller, N. Y. City.	1 Carcinoma. 2Epithelioma	Tongue, floor of mouth, glands of neck.	6 month
19	E. H....	M..	43	U. S.....	White.	Married	Butcher...	Private..	H. G. Bidwell, Jersey City, N. J.	1 Carcinoma. 2 Carcinoma ("rapidly growing and extremely malignant")	Rectum.....	3 month
20	A. G....	M..	58	U..S.....	White.	Married	.....	Private..	W. R. Bagley, Duluth, Minn.	1 Carcinoma. 2 Carcinoma.	Primary: Lower lip..... Secondary: Right side neck.	P r i m growth years; rence weeks.
21	I. S.....	F..	38	U. S.....	White.	Single..	Housework	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Left breast; *en cuirasse*; axillary and supraclavicular glands.	4 month
22	B. H....	F..	65	Irish.....	White.	Single .	Cook.....	Hospital.	.....	1 Carcinoma. 2 Carcinoma of scirrhus type.	Right breast.....	4 years.
23	N. S.....	M..	54	Italian.....	White.	Married	Laborer....	Hospital.	.....	1 Carcinoma. 2 Squamous-celled epithelioma.	Primary: Tongue..... Secondary: T o n g u e, cheek, glands of neck.	9 month
24	F. S.....	F..	55	English....	White.	Single..	Nun.....	Private..	G. V. Foster, N. Y. City.	1 Epithelioma (primary), carcinoma (secondary). 2 Carcinoma (secondary)	Primary: Vulva..... Secondary: Pelvic and inguinal glands, both sides; soft parts in femoral and inguinal regions.	5 years.
25	C. W. T..	M..	66	U. S.....	White.	Married	Soldier....	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Primary: Floor of mouth and glands of neck. Secondary: Tongue, cheek, throat.	4½ mo (secon
26	N. H. M.	F..	41	U. S.....	White.	Married	Church-worker.	Private..	Mary H. Brown, N. Y. City.	1 Carcionma. 2 Carcinoma.	Rectum.....	10 mon
27	M. F....	F..	66	U. S.....	White.	Single..	Teacher....	Private..	Eliza M. Mosher, Brooklyn, N. Y.	1 Sarcoma... 2 Small and large spindle celled sarcoma.	Primary: Left breast.... Secondary: Scar of previous operation; axilla, involving axillary vessels.	2 years.
28	F. H....	F..	41	U. S.....	White.	Married	Housewife.	Private..	.....	1 Carcinoma. 2.Carcinoma epithelioma.	Primary: Uterus..... Secondary: Vagina and pelvic glands.	1½ year
29	K. H....	F..	41	Irish.....	White.	Married	Housewife.	Hospital.	Daniel Cook, N. Y. City.	1 Carcinoma. 2 Carcinoma epithelioma.	Uterus (recurrent).....	1 year.
30	B. L....	F..	31	U. S.....	White.	Single..	.....	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Primary: Right breast... Secondary: Sternum and soft parts covering it.	4 years.
31	L. C	F..	19	U. S.....	White.	Single..	.....	Private..	C. B. Meding, N. Y. City.	1 Carcinoma.	Glands of neck.....	4 years.
32	H. L....	M..	59	Dane.....	White.	Single..	Laborer....	Hospital.	.....	1Epithelioma 2Epithelioma	Right inferior maxilla and glands of neck.	5 month

Previous Treatment	Condition When Enzyme Treatment was Begun	Duration of Enzyme Treatment	Effect Upon: 1 Local Condition 2 General Condition 3 Fetor 4 Pain 5 Progress of the Disease	Result
medication and local treatment ucorrhea (other physicians). curetted and packed with iodo-auze; laparotomy; disease irre-e; ovarian arteries ligated.	Extensive cancer of uterus uterus adherent to rectum; bladder involved.	Apr. 25 to June 3, 1907	1 Temporary improvement. 2 Temporary improvement. 3 Lessened at first. 4 Lessened. 5 Rapidity of growth apparently checked (improvement probably due to tying of vessels.)	Died June 24, 1907.
ilitic treatment (other physi-	Ulcerating mass involving right half of tongue; glands of neck enlarged; buccal cavity extremely foul.	Mar. 23 to June 2 1907	1 Buccal cavity cleaned up somewhat. 2 Temporary improvement. 3 Lessened. 4 Lessened. 5 None.	Died June 3, 1907 (hemorrhage).
nt for constipation, later for hoids (other physicians). Re-operation, when first seen. Jan. 3, 1907), consented to re-of tumor from rectum (Bain-	Enzyme treatment begun immediately after operation.	Jan. 5 to May 11, 1907.	Temporary improvement in general condition otherwise negative.	Died May 19, 1907
of growth on lower lip (Bag-emoval of glands of neck (Chas. *x*-ray (Bagley).	Large mass in inframaxillary region; irremovable. General condition good.	May 23 to Aug. 2, 1907. Full treatment (Bainbridge). After returning home, regime continued and 8 injections (Bagley). 12 injections (Fahey).	1 Temporary slight improvement. 2 Temporary improvement. 3 No fetor present. 4 None. 5 None.	Died Oct. 27 1907.
.....	Inoperable.....	Apr 3 to 29, 1908.....	Negative in all respects.	Died May 8, 1908.
efused operation. Operable....	Ulcerating tumor of right breast..	Nov. 10, 1907, to Jan. 26, 1908.	1 Ulcer became cleaner; some contraction. 2 Improved. 3 Lessened. 4 None. 5 None.	Discharged Dec. 20, 1907. Admitted to City Hosp., service of Dr. E.M. Foote, Finally consented to removal of tumor, Jan 27, 1908. Transferred to Metropolitan Hos. Backwell's Isl. on account of tuberculosis of lungs, May 15, 1908. Lost sight of
of growth on tongue, Feb, 1906 r hospital).	Inoperable, recurrent carcinoma..	Sept. 21, 1907 to Mar. 15, 1908.	Negative in all respects.	Died Mar. 17, 1908
of growth on vulva, Aug. 15, removal of inguinal glands, ge and packing of uterus, , 1906 (Bainbridge).	Patient convalescent from last operation; irremovable.	Nov. 5, 1906 to Jan. 13, 1907.	Hastened breaking down of growth and ulceration into femoral vessels, resulting in death from hemorrhage.	Died January 16, 1907.
ilitic treatment 3 mo., mouth ed (another physician). Ex-removal of diseased tissue, , 1906 (Bainbridge).	Mass size of marble in left submaxillary region; induration in floor of mouth.	Jan. 2 to Mar. 10, 1907.	Negative in all respects.....	Died Sept. 8, 1908.
ts for hemorrhoids; osteopathy hysicians).	Inoperable. Growth 3 inches from anus, extending up 6 inches.	Jan. 8 to July 26, 1907.	Marked temporary improvement in general condition (probably due to regime in hospital).	Died July 27, 1907
of breast, Feb., 1906. Axilla red. Recurrence in axilla with-ks, incised, Mar. 5, 1906 (other ns). First portion of sub-artery tied in order to control hemorrhages, Mar. 26, 1907 idge).	Irremovable, large, sarcomatous mass filling left axilla, fixed to chest wall, involving axillary vessels; mass size of large orange over scar of old operation hemorrhage profuse.	Apr. 3 to May 15, 1907.	Ulcerating surface cleaned up by lotio pancreatis; otherwise negative.	Died June 14, 1907.
tomy, Apr. 6, 1906 (another n). Removal of as much as of recurrent growth, Feb. 26, ainbridge).	Cauliflower-like mass involving site of hysterectomy and fornices of vagina; pelvic glands involved; general condition very poor; suffering from sepsis.	Dec. 22, 1906 to Feb. 19, 1907.	1 Improved for a time. 2 Markedly improved. 3 Lessened. 4 Lessened. 5 None.	Died, June, 1907.
growth removed June 2, 1906 r hospital).	Inoperable recurrent carcinoma of uterus.	Jan. 8 to Mar. 27, 1907.	Injections caused unusual pain. After a time trypsin was not absorbed promptly and several so-called "trypsin abscesses" were formed. Material removed from these proved to be unabsorbed trypsin. Negative in all respects.	Died Mar. 29, 1907
of right breast and axillary skin grafting, Nov. 3, 1906 idge).	Recurrence in sternum and soft parts covering it. Irremovable.	Mar. 13, 1908 to Apr. 11, 1908.	Negative in all respects.	Died during the summer, 1908.
.....	Enlarged glands in neck; neck measured 15½ inches.	Mar. 24 to Apr. 12, 1907.	Injections so painful patient refused to take treatment longer. Negative in all respects.	Died a few months later.
n refused.....	Ulcerated mass size of hen's egg attached to angle of lower maxilla submaxillary and sublingual glands involved; able to open mouth only slightly. Operable.	Sept. 17 to Dec. 20, 1907.	Negative in all respects.	Died Dec. 22, 1907

Case	Name	Sex	Age	Nationality	Color	Single or Married	Occupation	Private or Hospital	Referred by or in Consultation with	Diagnosis: 1 Clinical 2 Microscopic	Location of Disease	Durat Diseas vious Enz Treatm
33	H. G....	F..	38	German....	White.	Married	Housework	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Primary: Uterus..... Secondary: Abdominal viscera.	2 years
34	A. F....	F..	43	Irish.....	White.	Married	Housewife.	Private..	Edward F.Duffy, Yonkers, N. Y	1 Carcinoma. 2 Carcinoma.	Primary: Right brest.... Secondary: Left breast and skin. Uterine fibroid.	6 mon
35 Test Case	M. D....	F..	50	Canadian..	White.	Married	Housewife.	Hospital.	Emil Brunor, N. Y. City.	1 Carcinoma. 2 Carcinoma.	Uterus, broad ligaments, bladder, rectum, and pelvic fascia.	1 year.
36	I. S.....	M..	44	Russian....	White.	Married	Bartender..	Hospital.	.....	1 Ulcer of stomach, probably carcinomatous.	Stomach.....	8 years
37	S. S.....	F..	42	Russian....	White.	Married	Housewife.	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Primary: Right breast.. Secondary: Scar of operation, chest wall, axillary and supraclavicular glands, right side; left breast.	18 mon
38	E. S.....	F..	36	Hungarian.	White.	Married	Housewife.	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Uterus and broad ligaments.	7 mont
39	S. D.....	F..	38	U. S.....	White.	Married	Housewife.	Private..	.....	1 Carcinoma.	Left breast and axillary glands.	5 years
40	P. G....	M..	66	Irish.....	White.	Married	Engineer..	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Abdomen (probably mesentery and omentum) and abdominal wall.	2½ yea
41	M. M....	F..	56	Irish.....	White.	Single..	Housemaid	Hospital.	.....	1 Carcinoma. 2 Cacrinoma.	Stomach.....	16 mo
42	F. E....	M..	42	U. S.....	White.	Married	Newspaper work.	Private..	F. R. Johnson, Llewellyn Hatch.	1 Epithelioma 2 "Typical epidermoid cancer."	Tongue and glands of neck.	8 mon
43	K. M. W.	F..	45	U. S.....	White.	Married	Actress....	Hospital	.....	1 Carcinoma. 2 Carcinoma.	Left breast (1905)..... Right breast (1908).	4 m (r breas
44	G. U....	M..	47	German....	White.	Married	Printer....	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Left inguinal region and rectum.	9 mon
45	L. C.....	F..	40	U. S.....	White.	Married	Nurse.....	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Left breast and supraclavicular glands (recurrent).	2 yea mary m o (seco
46	N. C....	M..	62	Italian....	White.	Married	Restaurant keeper.	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Rectum.....	About
47	R. A. P..	F..	39	U. S.....	White.	Married	Housewife.	Private..	.....	1 Carcinoma. 2 Carcinoma.	Primary: Left breast.... Secondary: Scar and supraclavicular glands.	3 yea

Previous Treatment	Condition When Enzyme Treatment Was Begun	Duration of Enzyme Treatment	Effect Upon: 1 Local Condition 2 General Condition 3 Fetor 4 Pain 5 Progress of the Disease	Result
and packing of vagina (other ns); curettage, Dec. 3, 1907.	Irremovable. Cachexia marked; tissues involved very friable. General condition poor.	Dec. 21, 1907 to Jan. 24, 1908.	Negative in all respects. Disease continued to progress, involving abdominal viscera, as shown by exploratory laparotomy Feb. 26, 1908.	Died Feb. 27, 1908
ast removed, Aug. 13, 1907 X-ray twice a week for 2 mo. operation. Left breast, ax- d supraclavicular glands re- Dec. 17, 1907 (Bainbridge). very other day for several . G. Keith, Yonkers, N. Y.).	All external evidence of cancer removed. General condition good.	Dec. 27, 1907 to Mar. 11, 1908. Continued several weeks by Dr. James T. Gorton, Yonkers, N. Y.	1 Some of the secondary nodules disappeared and others decreased in size. 2 Marked improvement. 3 No fetor present. 4 Apparently controlled, certainly not increased. 5 Did not prevent metastasis or recurrence.	Died June 16, 1908.
right breast removed in 1902 physician). Tubes and emoved, both ovarian arteries . 5, 1907 (Bainbridge).	Irremovable carcinoma of structures involved.	Internal medication and hypodermic injections of glycerin and water, Dec. 13 to 29, 1907. Regular enzyme treatment continued by Dr. Emil Brunor, Nov. 26, 1907 to Apr. 26, 1908.	Under control treatment steady improvement in general condition. Began to fail as soon as the injections of trypsin and amylopsin were begun. No metastases after beginning enzyme treatment.	Died Apr. 27, 1908
tomy, 1900; gastro-enteros- 01; plastic operation for en- contracted gastro-enteric ori- ; medical treatment for per- omiting, 1907 (another hos- xploratory laparotomy, gas- ostomy, Mar. 30, 1908 (Bain-	Persistent vomiting; pain in epigastrium. Chronic gastric ulcer with peritoneal adhesions.	Feb. 27 to Mar. 26, 1908.	Negative in all respects.	Died May, 1908.
right breast removed, Sept. other physician). Radical re- f right breast and enlarged nd supraclavicular glands of e; removal of small nodule er portion of left breast, Nov. (Bainbridge).	Irremovable involvement of chest wall.	Nov. 11, 1906 to Feb. 6, 1907.	Improvement of general condition, attributable to operation. Progress of disease not checked.	Discharged from hospital, Feb. 6, 1907. Not able to trace subsequent history.
and application of zinc Mar. 21, 1907 (Bainbridge).	Irremovable. Suffering from sepsis; cachexia marked.	Mar. 19 to May 24, 1907.	1 Improved. 2 Less septic, less cachectic. 3 Lessened. 4 None. 5 None. Improvement doubtless due to regime rather than to the injections.	Discharged from hospital, May 24, 1907. Unable to trace subsequent history.
Refused operation.....	Large ulcerating tumor in left breast and one in axilla; arm very much swollen; pain intense.	Apr. 28 to May 27, 1907.	Complained of pain from injections. Negative in all respects.	Discontinued treatment at patient's request, May 27, 1907. Lost sight of.
ıcised, Aug., 1906 (another	Tumor extending from umbilicus to symphysis pubis, hard, irregular, slightly nodular. Just below umbilicus a discharging sinus resulting from operation.	May 5 to June 3, 1907..	Slight apparent improvement in general condition at first.	Discharged from hospital by request June 3, 1907. Lost sight of.
medical (other physicians). ory laparotomy, Feb. 11, inbridge).	General condition poor. Operation showed large, hard growth connecting stomach, pancreas and colon.	Feb. 14 to Apr. 28, 1907.	Decided improvement in general condition.	Discharged by request, improved, Apr. 29, 1907. Lost sight of.
c treatment 3 mo.; 11 caustic ns (other physicians). Ex- dissection of broken down neck and involved sheaths of nternal jugular vein ligated, 906; both sides of neck curett- inferior maxillary division of posterior auricular nerves cut pain, Jan. 17, 1907 (Bain-	Ulcerating cancer of tongue, too far advanced to warrant removal of tongue.	Dec. 11, 1906 to Jan. 14, 1907.	Apparent temporary improvement both local and general. Autopsy showed no metastases, despite extensive involvment.	Died Jan. 20, 1907
noved from left breast, 1905; moval of left breast and axil- ds, Sept., 1907 (other hospi- ical removal of right breast ry glands, Apr. 2, 1908 (New n and Cancer Hospital).	Enzyme treatment begun two weeks after last operation, to prevent metastasis.	Apr. 15 to 24, 1908. Large doses.	Negative in all respects.	Discharged by request, Apr. 25, 1908. Lost sight of.
for fissure of rectum, June 6, loratory laparatomy, left in- lostomy, July 15, 1907 (an- pital).	Tumor in rectum, 3½ inches from anus; left inguinal glands enlarged. Inoperable.	Jan. 10 to 31, 1908....	Temporary improvement in general condition. Otherwise negative.	Discharged Jan. 31, 1908, steadily growing worse. Died later.
t and supraclavicular glands July 16, 1906 (another	Recurrence in scar of breast amputation; arm and hand greatly swollen and very painful. Operation refused.	Mar. 1 to May 7, 1908.	Negative in all respects. Treatment painful when large injections were used.	Refused further treatment. Discharged Mar. 8, 1908. Lost sight of.
ds removed by cautery, Sept. ther physician). Rectum di- n. 19, 1907 (Bainbridge). peration refused.	Nodular masses for a distance of 3 inches in rectum; annular mass extending 2 inches further. Pain, constipation, bloody stools.	Nov. 18, 1906 to Apr. 16, 1907.	1 Discharge from rectum freer; obstruction not so marked. 2 Temporarily improved. 3 Lessened. 4 Lessened. 5 None.	Died Mar., 1908.
f breast, Feb., 1906 (another . Refused further operation.	Irremovable. Considerable pain. General condition fair.	Feb. 19, 1907 to Apr. 27, 1907.	1 Distinct improvement. Some nodules apparently disappeared and others decreased in size and became softer. 2 Gained 17 lb. in less than 1 mo. 3 Lessened. 4 Lessened for a time. 5 Seemingly retarded.	Discontinued treatment voluntarily Apr. 27, 1907. Died several months later.

Case	Name	Sex	Age	Nationality	Color	Single or Married	Occupation	Private or Hospital	Referred by or in Consultation with	Diagnosis: 1 Clinical 2 Microscopic	Location of the Disease	Dura Dis Previ En Trea
48	A. B....	M..	45	U. S.....	White.	Married	Conductor.	Hospital.	.....	1 Carcinoma.	Tongue and glands of neck (recurrent).	4 mon
49 Test Case	F. D....	F..	20	U. S.....	White.	Single..	.....	Private..	C. A. Frink, N. Y. City.	1 Goitre.... 2 Goitre.	Neck.....	
50	M. T....	F..	65	U. S.....	White.	Single..	Seamstress.	Hospital.	W. E. Cladek, Rahway, N. J.	1 Carcinoma.	Right breast.....	12 yea
51	B. H....	M..	93	Irish.....	White.	Married	.....	Private..	.....	1 Epithelioma 2 Epithelioma	Right auricle.....	10 yea
52	J. E. W..	M..	52	Swede.....	White.	Married	Laborer....	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Right side of face, outer angle of orbit, over malar and zygoma.	7 yea
53	A. D....	F..	54	German....	White.	Married	Housewife.	Hospital.	.....	1 Epithelioma 2 Epithelioma (foot) carcinoma (glands).	Foot and inguinal glands; femoral abscess.	3 mon
54	C. E. C..	F..	46	Canadian..	White.	Married	Housework	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Primary: Right breast, glands of neck and axilla Secondary: Chest wall, left breast.	Prima years Secon mon
55	J. M....	M..	76	Irish.....	White.	Married	Laborer....	Hospital.	.....	1 Carcinoma.	From base of tongue to hyoid bone; epiglottis; larynx; glands of neck.	5 mon
56	J. P.....	F..	48	Irish.....	White.	Single..	Housework	Hospital.	.....	1 Epithelioma 2 Epithelioma	Auricular region (recurrent.)	Prima years rence
57	A. R....	F..	54	U. S.....	White.	Married	Housework	Hospital.	.....	1 Carcinoma.	Stomach.....	1 yea
58	L. D....	F..	34	German....	White.	Married	Housewife.	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Primary: Left pectoral region. Secondary: Left pectoral region, shoulder and back.	6 mon
59	S. R.....	F..	56	Roumanian	White.	Married	Housewife.	Hospital.	.....	1 Sarcoma...	Bladder.....	5 mon
60	A. W....	F..	35	U. S.....	White.	Married	Housewife.	Private..	.....	1 Carcinoma. 2 Carcinoma.	Primary: Uterus and broad ligaments. Secondary: Pelvis, glands along aorta and iliacs.	3 yea
61	A. L....	F..	77	Irish.....	White.	Married	Housewife.	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Primary: Left breast.... Secondary: Axilla; later in scar and supraclavicular glands.	1 mo curr
62	W. C....	F..	45	U. S.....	White.	Married	Housewife.	Private..	T. J. Dunn, N. Y. City.	1 Carcinoma. 2 Carcinoma.	Primary: Uterus..... Secondary: Pelvis and vault of vagina.	4 yea
63	L. R. D..	F..	....	U. S.....	White.	Married	Housewife.	Private..	L. A. Opdyke, Jersey City, N.J.	1 Carcinoma.	Uterus.....	
64	S. S. T..	M..	....	U. S.....	Colored	.....	Laborer....	Private..	H. E. Hale, N. Y. City.	1 Carcinoma.	Stomach.....	3 mo
65	G. G....	F..	35	U. S.....	White.	Married	Housewife.	Private..	B. H. Mayne, R. Byington, Brooklyn, N. Y.	1 Carcinoma.	Uterus.....	1 yea

Previous Treatment	Condition When Enzyme Treatment Was Begun	Duration of Enzyme Treatment	Effect Upon: 1 Local Condition 2 General Condition 3 Fetor 4 Pain 5 Progress of the Disease	Result
al of growth from tongue, one later, removal of a larger section tongue, and supraclavicular s, Aug., 1907 (another hospital).	Large mass behind ramus of left; jaw, extending to symphysis; ulcer on right side of tongue, right side of neck swollen. Irremovable.	Nov. 1 to 9, 1907.....	Pain seemingly increased. Otherwise negative.	Discharged by request Nov. 9, 1907. Died later.
.....	Large parenchymatous goitre.....	Mar. 4 to Apr. 30, 1907. Large doses of trypsin and amylopsin.	Painful indurated areas at sites of injection. No effect upon the goitre, which was removed May 24, 1907 (Bainbridge).	Uneventful recovery from operation; perfectly well May 17,1909.
.....	Nodular mass size of walnut over nipple of right breast; slight ulceration, no discharge; axillary glands enlarged. Operable, operation refused.	Dec. 7, 1907 to Feb. 27, 1908, in hospital, and irregularly for 8 mo. after returning home (Cladek).	Gained 10 lb. in weight while in hospital; appetite improved. Progress of the disease seemingly retarded but not stopped.	Discharged Feb. 27, 1908. May 12, 1909, patient able to do light housework. Disease slowlyprogressing
a few times, radium, 2 months physicians). No operation.	Ulcerating growth involved entire auricle and contiguous postauricular area.	Feb. 8 to May 12, 1908.	1 Ulcerating surface cleaned up. 2 None. 3 None. 4 Lessened for a time. 5 None.	Insisted upon discontinuance of injections because of pain. Still under observation. Disease gradually progressing.
incised and packed, 3 mos. after ppearance (another hospital). r removed by plaster a short time this (another physician). No re- ntil Mar., 1907, when a blow was ed on the temple. Soft tissues ed, portions of the malar, frontal perior maxilla removed, the right ll enucleated and the orbital fossa d out, Dec. 12, 1907 (Bainbridge)	Patient recovering from operation when treatment was begun. Irremovable in part.	Dec. 21, 1907 to Jan. 16, 1908. No injections given; all otner parts of treatment as usual.	Seemed to gain for a time. Injections painful. Grew progressively worse.	Died Apr. 10,1908
n on foot removed, enlarged in- l glands excised, and femoral ss evacuated, Mar. 25, 1908 bridge).	Suffering from absorption of toxic products; general condition very poor.	Apr. 6 to 19, 1908.....	Negative in all respects.	Discharged by request May 2, 1908. Died a few days later.
in breast opened as an abscess, 2 years ago (another physician); al of left breast, about 2 months (another hospital). Axillar and clavicular glands and mass in breast not removed.	Numerous small masses over chest wall; large discharging mass over site of left breast; glands in neck and axillæ markedly enlarged. Inoperable except for paracentesis for removal of fluid from chest cavity.	Nov. 6 to Dec. 26, 1907	Reaction very severe; no beneficial effects; treatment abandoned because of patient's weakened condition.	Died Jan. 26, 1908
.....	Carcinomatous masses extending from base of tongue to hyoid bone involving epiglottis and larynx, interfering with deglutition. Inoperable.	Jan. 3 to Mar. 8, 1908..	Negative in all respects.	Died Apr. 3, 1908.
al of primary growth in 1903 her hospital)	Irremovable ulcerating growth involving the tissues named.	Jan. 9, to Sept. 18, 1908. (Injections 2 months, internal treatment 9 months).	1 Ulcerated surface on cheek decreased in size, floor cleaner and healthier. 2 Improved temporarily. 3 Lessened. 4 Lessened. 5 Growth seemed to be checked to some extent at first, later disease progressed rapidly.	Removed to Bellevue Insane Pavilion Sept. 18, 1908. Died shortly after.
al treatment 4 months. Operafused.	Characteristic symptoms of cancer of stomach.	Jan. 2 to May 9, 1907..	Improved, probably because of the 4 months' hospital régime and treatment.	Discharged by request May 9, 1907.
al of left breast (1900) (another al). Removal of foci in chest part of sternum and ribs over extensive operations (four) in nd 1907 (Bainbridge).	No disease apparent.....	Dec. 12, 1906 to May 10, 1907. (To prevent recurrence).	General condition improved. Considerable local pain not influenced.	Discharged May 11, 1907. Received electrical treatment for 3 mos. after leaving hospital. No recurrence at present.
l for cystitis (another physician).	Hemorrhages from bladder; incontinence of urine.	June 1 to July 15, 1907.	Negative in all respects.	Died Aug. 14, 1907.
terectomy, Nov. 2, 1905 (Bain-).	Inoperable.....	Feb. 4 to Aug. 17, 1907. Jan. 16 to Apr. 7, 1908.	General condition much better for a number of months. Treatment seemed definitely to prolong life. Disease steadily progressed.	Died Apr. 18, 1908
l operation for removal of left , June, 1906 (another hospital). cleared, June 20, 1907 (Bain-). Further operation refused.	Recurrence in scar of breast amputation.	Dec. 10, 1907 to Jan. 10, 1908. Further treatment refused.	Negative in all respects.	Died May 30, 1908
l hysterectomy, Oct., 1906 ier hospital).	Mass in pelvis size of fist; ulcerated surface at vault of vagina. Anemic, otherwise general condition good. Irremovable.	3 weeks, small doses (Dunn). Jan. 15 to Feb. 12, 1907 (Bainbridge). Full doses.	Only effect, increase in discharge from ulcerating surface in vault of vagina.	Died Apr. 4, 1907.
ve (other physicians).....	Inoperable.....	Feb. to May, small doses. May 9 to 24, 1907. Refused further treatment.	Negative except that it seemed to relieve pain for a time.	Died June 3, 1907
.....	Mass in epigastric region; hemorrhages from stomach.	Jan. 23 to Mar. 11, 1907.	Negative except for improvement in digestion.	Died Apr. 24, 1907
of tumor curetted (another ian).	Large inoperable uterine cancer. Patient confined to bed.	Jan. 18 to Feb. 15, 1907.	Improvement in general condition for a few days; discharge increased. Otherwise negative.	Died Feb. 16, 1907

Case	Name	Sex	Age	Nationality	Color	Single or Married	Occupation	Private or Hospital	Referred by or in Consultation with	Diagnosis: 1 Clinical 2 Microscopic	Location of the Disease	Duration Disease Previous Enzym Treatme
66	R.H.F...	F..	58	U. S.....	White.	Married	Housewife.	Private..	R. F. Ives, Bath Beach, L. I.	1 Carcinoma.	Entire left breast, involving ribs, axilla and side of arm; right breast.	6 years.
67	G. G. D..	F..	60	U. S.....	White.	Married	Housewife.	Private..	J. P. Green, Mamoroneck, N. Y.	1 Carcinoma.	Primary: Left breast..... Secondary: Skin over left breast; right breast, axillary glands, and skin of right side.	1 year.
68	A. S...	F..	32	U. S.....	White.	Married	Housewife.	Private..	J. Ziporkes, Brooklyn, N. Y.	1 Carcinoma. 2 Carcinoma.	Primary: Uterus..... Secondary: Pelvis.	8 months
69	M. O....	F..	39	U. S.....	White.	Married	Housewife.	Private..	W. F. Faison, Jersey City, N. J.	1 Sarcoma... 2 Sarcoma, large spindle celled.	Right breast (recurrent)	14 years.
70	M. P. S..	F..	54	U. S.....	White.	Married	Housewife.	Private..	L. H. Clarke, Holyoke, Mass.	1 Carcinoma. 2 Carcinoma.	Primary: Left breast..... Secondary: Scar and axilla.	4½ years.
71	R. H....	F..	50	U. S.....	White.	Married	Housewife.	Private..	.....	1 Carcinoma.	Liver.....	Several m
72	G. H. S..	F..	43	U. S.....	White.	Married	Housewife.	Private..	A. C. Benedict, Yonkers, N. Y.	1 Carcinoma. 2 Carcinoma.	Neck, left side.....	5 years.
73	W. D....	M..	45	U. S.....	White.	Married	Clerk.....	Hospital.	.....	1 Epithelioma. 2 Epithelioma.	Primary: Left ankle, near external malleolus. Secondary: Abdominal viscera and inguinal glands.	1 year.
74	E. K. G.	M..	37	U. S.....	White.	Married	Salesman..	Private..	.....	1 Carcinoma. 2 Carcinoma.	Primary: Tongue and glands of neck. Secondary: Floor of mouth and neck.	2 years.
75	E. R. T..	F..	50	U. S.....	White.	Married	Housewife.	Private..	J. P. Green, Mamaroneck, N. Y.	1 Carcinoma.	Uterus and base of bladder.	About 1
76	E. S.....	M..	42	U. S.....	White.	Married	Salesman..	Private..	I. P. Oberndorfer, New York City.	1 Carcinoma. 2 Carcinoma.	Primary: Tongue..... Secondary: Neck, throat, back.	8 years.
77	F. E. G..	F..	39	U. S.....	White.	Married	Singer.....	Private..	John Beard, Edinburg, Scotland; Robert Ives, Bath Beach, N. Y.	1 Carcinoma. 2 Carcinoma.	Primary: Uterus..... Secondary: Pelvis.....	2 years.
78	A. S.....	F..	48	Irish.....	White.	Married	Clerk.....	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Primary: Left breast..... Secondary: Skin over area of operation; supra- and infraclavicular glands.	2 years.
79	M. F....	F..	50	Italian....	White.	Married	Seamstress.	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Primary: Uterus..... Secondary: Vagina.....	2 years.
80	F. D....	F..	49	U. S.....	White.	Married	Housewife.	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Uterus and bladder.....	Symptor noted b tient o weeks.
81	E. C.....	F..	44	Irish.....	White.	Married	Housewife.	Hospital	.....	1 Carcinoma. 2 Carcinoma.	Left breast.....	16 mont
82	E. D....	M..	61	Irish.....	White.	Married	Clerk.....	Hospital.	.....	1 Epithelioma. 2 Epithelioma.	Buccal cavity (recurrent)	Primary and a years. Secondar months
83	E. D....	F..	30	Russian....	White.	Married	Housewife.	Hospital.	.....	1 Carcinoma.	Primary: Left breast..... Secondary: Skin over site of operation; axilla.	2 years.

Previous Treatment	Condition When Enzyme Treatment Was Begun	Duration of Enzyme Treatment	Effect Upon: 1 Local Condition 2 General Condition 3 Fetor 4 Pain 5 Progress of the Disease	Result
ovinine (other physicians). No on.	Inoperable. General condition fair.	Dec. 28, 1906 to Mar. 27, 1907.	Negative in all respects.	Died later.
l of tumor in left breast (another an).	Small injections of trypsin (10) and amylopsin (2) during Oct., 1907. (Green). Dec. 26, 1907 to Feb. 21, 1908.	Oct. 5, 1906 to Feb. 21, 1907. Small injections at first, gradually increased.	Tumor in right breast disappeared, but returned again. Disease steadily progressed.	Died Feb. 21, 1907
tomy, 1906 (another hospital).	Recurrent tumor in pelvis; very painful; general toxemia from failure of emunctory organs to functionate.	Apr. 17 to June 16, 1907.	Gained 5 lb. in weight; much stronger; less pain at first. Progress of disease not influenced.	Died June 16, 1907
lanced three times (another an). Breast and axillary glands d, Aug., 1906 (Faison). X-ray nes in Feb., 1907.	Ulcerating sarcoma; profuse hemorrhage; weak; emaciated.	Mar. 2 to Apr. 2, 1907.	Negative in all respects.	Died Apr. 3, 1907.
e removal of breast and glands a, Apr., 1903, X-ray 2 years er (Clarke). Radium a few days r physician). Removal of res, Nov. 7, 1907 (Bainbridge). ecurrent nodule removed under anesthesia, Jan. 9, 1909 (Bain-	Small discharging sinus in axilla; recurrent nodules in skin; general condition good; contraction of scar and edema of arm.	Nov. 25, 1907 to Feb. 26, 1908. Given in the hope of preventing metastasis. June 2 to July 14, 1908.	Did not prevent recurrence. Whether it influenced extent of recurrence cannot be determined.	Free from apparent disease, May 12, 1909.
.....	Liver very much enlarged. Progressive loss of appetite, strength and weight; nauseated all the time.	Dec. 22 to 27. Refused further treatment.	Negative. Patient complained of the pain of injections.	Died a few weeks later.
intervals, palliative treatment, hree times a week for nine weeks, Relieved pressure by exploraperation, Dec. 6, 1906 (Bain-	Tumor pressing upon superior laryngeal nerve: paralysis of left side of face. Difficult deglutition.	Dec. 9, 1906 to May 6, 1907.	1 Growth in neck decreased in size. 2 Improved. Able to swallow more easily; facial paralysis less marked. 3 None present. 4 Lessened. 5 Retarded; life prolonged.	Died May 15, 1907
l of growth on ankle, June 22, Refused to allow removal of l glands, until Mar. 10, 1908.	Recurrence in abdominal viscera. General condition fair.	Dec. 1, 1907 to Feb. 14, 1908.	Negative in all respects. Did not prevent metastasis, as autopsy showed metastases in all the abdominal viscera.	Died Mar. 12, 1908
ation (alum stick); treated for losis (other physicians). Reof tongue and glands of neck 907 (Bainbridge).	Inoperable recurrence in floor of mouth and neck. Thin and cachectic. Pain severe.	Feb. 27 to May, 8, 1908.	Negative in all respects	Died May 10, 1908
tonic treatment; uterus cauternother hospital).	Inoperable carcinoma of uterus and bladder. Constipation, frequent urination, severe pain.	From Oct. to Dec., 1907 received 10 injections trypsin and 2 amylopsin, then liquid glycerin trypsin (Green). Holadin, oxgall and dietary regime from Dec. 26, 1907, to time of death, some six weeks later.	Distinct evidence of depression after small injections of trypsin. Negative except for temporary general improvement.	Died some weeks later (early in 1908).
hilitic treatment for a number nths; X-ray three times (other ans). Removal of tongue and of neck, Mar. 1907 (Bainbridge).	Recurrence in neck, throat and back. Septic looking, emaciated, exceedingly nervous.	Mar. 23 to Sept 26, 1907.	Pain seemed to be increased by treatment. No favorable effect. Disease steadily progressed.	Died May 3, 1908.
ctomy, Apr., 1906 (another an).	Extensive involvement of pelvis. General condition very poor.	Nov. 7 to 19, 1906....	Negative in all respects.	Died Nov. 21, 1906.
e amputation of breast Apr. 8, nother hospital).	Inoperable recurrence in scar of operation, nodules in surrounding skin; supra- and infraclavicular glands. Arm greatly swollen.	July 1, 1907 to Nov. 2, 1908.	Improved under regime for a time.	Died some months later.
ctomy, Aug. 23, 1905 (another l).	Neuralgic pains in left hip and leg. Small ulcerated area in vagina. Operation refused.	Jan. 13 to Apr. 12, 1907.	Negative. Disease steadily progressed.	Died Apr. 3, 1908.
curetted; ovarian and uterine , both sides, ligated, Apr. 18,	Extensive involvement of uterus, broad ligaments and bladder found upon exploration. Irremovable.	May 6 to Nov. 2, 1908.	Temporary check to growth, as indicated by symptoms, probably due to ligation of vessels.	Discharged, improved, June 4, 1908. Disease slowly progressing but patient able to do light housework.
t (family physician). Refused on.	Hard, eroded tumor in breast; nipple retracted. Progressive loss of flesh and strength.	Apr. 1 to July 1, 1908..	Lost 15 lb. in weight while on the treatment. Negative.	Died July 7, 1908.
growth, with free margin of tissue, excised, July 21, 1906 al).	Extensive involvement of buccal mucous membrane; foul discharge; intense pain.	Apr. 3 to Sept. 19, 1908. Refused further treatment.	Negative in all respects.	Died in few weeks later.
amputated, July, 1906; recurn scar excised, Feb. 10, 1908 er hospital).	Induration of edges of wound from last operation, which never healed. Eroded area 3 inches long in axilla, with protruding ulcerating mass.	March 25 to June 1, 1908.	1 Wound cleaned up by Lotio Pancreatis. Discharge increased. 2 Loss of weight; increased cachexia. 3 Lessened. 4 None. 5 None.	Died Dec. 1, 1908.

Case	Name	Sex	Age	Nationality	Color	Single or Married	Occupation	Private or Hospital	Referred by or in Consultation with	Diagnosis: 1 Clinical 2 Microscopic	Location of Disease	Duration Disease Previous Enzym Treatm
84	T. D....	M..	51	U. S.....	White.	Married	Laborer....	Hospital.	.....	1 Carcinoma.	Neck (recurrent.).....	1 year.
85	W. D....	M..	57	U. S.....	White.	Married	Engineer...	Private..	J. Fewsmith, Newark, N. J.	1 Epithelioma. 2 Epithelioma.	Tongue.....	6 months
86	J. H. W.	M..	60	U. S.....	White.	Married	Clerk.....	Hospital.	Alfred C. Prentice, New York City.	1 Carcinoma. 2 Epithelioma.	Glands of neck.....	1 year
87	M. R....	F..	44	Irish.....	White.	Married	Housework	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Uterus and vagina.....	4 months
88	M. C....	F..	65	Irish.....	White.	Married	Housewife.	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Right breast.....	2 years.
89	R. G....	F..	48	Russian....	White.	Married	Housewife.	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Right breast; glands of neck.	6 months
90	M. E....	F..	71	German....	White.	Married	Housewife.	Hospital.	Geo. Forbes, L. I. City, N. Y.	1 Carcinoma.	Left tonsil; glands of neck.	4 months
91 Control Case	S. H....	F..	51	U. S.....	White.	Married	Housewife.	Hospital.	.....	1 Carcinoma.	Abdominal viscera.....	
92 Control Case	A. A....	F..	57	Irish.....	White.	Married	Housewife.	Hospital.	.....	1 Epithelioma. 2 Epithelioma.	Chin and inferior maxilla.	10 years.
93	M. S....	F..	55	Irish.....	White.	Single..	Domestic..	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Primary: Right breast... Secondary: Skin over site of breast; glands of neck and axilla.	5 years.
94	F. W....	F..	39	U. S.....	White.	Married	Housewife.	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Primary: Rectum and vagina. Secondary: Uterus, ovaries, tubes, broad ligaments.	6 month
95	E. O....	F..	51	Dane.....	White.	Married	Housework	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Primary: Uterus..... Secondary: Inguinal glands, hip, thigh.	Primary months Seconda weeks.
96	M. R....	F..	36	Dane.....	White.	Married	Housework	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Uterus and bladder.....	7 month
97	M. W....	M..	48	Irish.....	White.	Married	Factory work	Hospital.	.....	1 Carcinoma. 2 Epithelioma.	Left submaxillary region and glands of neck (recurrent).	1½ years
98	G. R. E..	F..	62	U. S.....	White.	Married	Housewife.	Private..	.....	1 Carcinoma.	Primary: Pharynx..... Secondary: Larynx; glands of neck.	9 month
99	A. W....	F..	44	U. S.....	White.	Married	Housewife.	Hospital.	.....	1 Carcinoma. 2 Carcinoma.	Right breast.....	1 year.
100	A. B....	M..	69	U. S.....	White.	Married	Laborer....	Hospital.	R. C. Kemp, New York City	1 Carcinoma.	Stomach (superimposed upon gastric ulcer).	2½ years

Previous Treatment	Condition When Enzyme Treatment Was Begun	Duration of Enzyme Treatment	Effect Upon: 1 Local Condition 2 General Condition 3 Fetor 4 Pain 5 Progress of the Disease.	Result
of primary growth, Jan., 1906 r physician). Curetted ulcer- urface, June 14, 1906. (Bain-	Ulcerating mass in neck below mastoid process. Very fetid.	Oct. 24, 1906, to March 19, 1907.	Negative in all respects.	Died Mar. 20, 1907
m Iodid; cauterization (Few- Amputation of tongue, April 8. Removal of cystic tumor, avicular region, May 4, 1908. idge.)	Treatment begun after second operation.	May 20 to June 12, 1908.	Negative in all respects.	Died later.
tive interference.....	Glands of neck broken down, ulceration extending to tongue and buccal mucous membrane. Inoperable.	Feb. 10 to Oct. 4, 1908. Discontinued at patient's request.	Negative in all respects.	Alive Jan., 1909. In fairly good condition.
.....	Irremovable, ulcerating tumor involving uterus and vagina. Loss of 20 pounds in weight in four months; fetid bloody vaginal discharge.	April 10 to June 27, 1908. No injections.	Lotio Pancreatis caused slight temporary improvement in fetid discharge. Otherwise negative.	Discharged by request June 27, 1908. Died later.
peration refused.....	Large mass in breast; nipple retracted; axillary glands enlarged. Operable.	June 1 to Nov. 2, 1908	Negative in all respects. Development of disease very slow but progressive.	Alive April 26, 1909. About the same as when treatment was discontinued.
peration refused.....	Hard mass size of orange in breast; glands of neck carcinomatous.	March 13 to Oct. 2, 1908. Discontinued at patient's request.	Negative in all respects.	Lost sight of.
Operation refused.....	Hard mass size of orange in neck.	May 1 to June 15, 1908. Discontinued at patient's request.	Negative in all respects.	Discharged June 20, 1909. Died later.
.....	Inoperable. Cachectic, weak, emaciated; vaginal discharge; pain in back.	Jan. 13 to April 11, 1908, injections of sterile water, and the internal treatment. April 11 to May 1,1908, full Trypsin treatm't.	Did as well upon the injections of sterile water as upon the trypsin and amylopsin injections. Negative.	Died July, 1908.
vashes, X-ray, at intervals for years (other physicians). Re- f involved soft parts and por- lower maxilla, 1908. (Bain- April 18, several subsequent ents of granulating surface and of necrotic tissue (hospital). l of diseased soft parts and re- f 2 inches of central portion of axilla; plastic operation, Dec. 8. (Bainbridge.) Removal of bone, Jan. 19, 1909. (Bain-	Treatment begun after second operation (June 3, 1908) for removal of necrosed bone.	Sterile water injections and regime, June 3 to 19, 1908. Dietary regime, with occasional resort to the internal medication, continued during stay in hospital.	General condition improved, probably due to regime. Disease progressed, despite frequent operations.	Discharged, improved, Feb. 9, 1908.
emoved, June, 1906 (another). Recurrence in chest wall outer surface of ribs and costages curetted, April 13, 1908; vicular region explored and encroaching upon carotid and an dissected out, May 18, 1908. dge.)	Treatment begun after second operation.	June 18 to 30, 1908. Discontinued at patient's request.	Injections very painful. Negative.	Discharged July 1, 1908; improved (from operation). Lost sight of.
rectal wall and diseased por- agina exsected, June 25, 1907; aries and tubes removed, both arteries ligated and both broad s constricted by ligature near all, Feb. 7, 1908. Further op- procedure impossible. Bain-	Treatment begun shortly after second operation; patient in better condition than before.	Feb. 24 to July 31, 1908. (Irregularly.)	Negative in all respects.	Died Aug. 17, 1908.
omy, Dec., 1906 (another).	Mass in groin attached to ileum..	Feb. 26 to April 14, 1908.	Negative in all respects	Died June 16,1908
phorectomy; ligation of ovar- terine arteries, April 27, 1908; of masses from vaginal wall ix, May 25, 1908. (Bainbridge)	Irremovable; condition improved as result of operation.	June 8 to July 31, 1908, regular treatment. July 31 to Aug. 30, 1908, trypsin per rectum.	Negative in all respects.	Died Sept. 1, 1908.
growth removed, Oct., 1906 hospital). Removal of as possible of diseased tissue, , 1908. (Bainbridge.) Ex- of submental, submaxillary erior carotid triangles; liga- ft external carotid, sublingual, thyroid, ascending pharyn- al, and posterior occipital ar- pril 11, 1908; subsequent in- f right carotid with paraffin. dge.)	Treatment begun immediately after ligation of arteries. Irremovable.	April 13 to July 23, 1908.	Negative in all respects.	Discharged by request, July 24, 1908.
my (another physician).....	Dyspnea; general condition poor	Dec. 19, 1907, to June 16, 1908. Large doses.	Improved somewhat for a time; pain lessened.	Died July 2, 1908.
efused operation.....	Tumor in breast hard and livid, involving entire gland.	July 20 to Dec. 11, 1908	Malaise, insomnia and pain seemed definitely increased by the injections.	Discharged Dec. 11, 1908. Lost sight of.
and dietetic. Refused op-	Anemic, cachectic, progressively losing weight. Tumor size of hen's egg in body of stomach.	May 6 to July 8, 1908..	Tumor decreased in size; pain alleviated; gained 20 pounds in weight; returned to work.	Died a few months later from pneumonia.

PROSPECT AND RETROSPECT

In my previous paper on Trypsin attention was directed to the fact that it should always be borne in mind, in testing a so-called cure for cancer, that between the starting point, "no evidence," and the hoped for goal, "a cure," there may be many way stations of usefulness. In the trial of the Enzyme Treatment we have kept this ever in mind. While, unfortunately, we have not reached the goal of either prevention or cure, we believe there are several way stations of usefulness along the route.

The internal medication and the local solvent have their place as adjuvants in the cure of the patient afflicted with cancer; the dietary regime, forced feeding when necessary, exercise, and fresh air do much in these cases, as in other chronic conditions, to ameliorate the ravages of the disease. The trypsin and amylopsin, though employed in every manner suggested by Dr. Beard, have not, in our experience, substantiated the claims of curative and preventive properties advanced for them. Whether trypsin will be found to be of the diagnostic value which some of the German workers have predicted remains for further tests and more extended research to determine.

Looking back upon the work of the last three years, the most important lesson to be drawn from the test of the Enzyme Treatment of cancer is that the patient is a human being who, while suffering from cancer, it is true, may at the same time be the subject of any of the other ills to which flesh is heir, and who doubly deserves to be treated with all the careful scientific attention which modern medicine and surgery command. By building up the nutrition, aiding the impaired function of elimination, treating complications, giving to the patient a better mental as well as physical atmosphere,—in other words, treating the patient and not the "cancer case,"—suffering can be wonderfully ameliorated and life, in many instances, prolonged in comparative comfort for months and even years.

SUMMARY

From careful clinical and laboratory observations, extending over a period of three years, the following deductions may be drawn:

(1) That the internal medication with Holadin and oxgall aids digestion and increases elimination.

(2) That lotio pancreatis applied locally clears the ulcerating surface by removing organisms, thus aiding in diminishing the absorption of their products.

(3) That aiding digestion, increasing elimination (by skin, kidneys, and bowels), and decreasing local absorption are the most important features of the treatment.

(4) That the regime by increasing resistance may in some cases decrease the rapidity of the malignant process.

(5) That control cases given injections of glycerin and water or sterile water alone, plus the regime, did as well as those on the full enzyme treatment.

(6) That injectio trypsini, in some cases, seems to cause more rapid disintegration of (to "liquefy," according to Beard) cancerous tissue.

(7) That while it may accelerate the breaking down in the center of the tumor mass, the periphery is found to be actively growing, as was true of Case VII (Case I of Dr. Morton's published series). When injected into the tumor itself this disintegration is more marked.

(8) That because of the tendency of injectio trypsini to disintegrate the tissues, it may be a direct menace to life (*a*) by eroding large blood vessels (when the disease is contiguous to these structures, as when deep in the neck or in the pelvis), thus causing death from hemorrhage; (*b*) when given in large doses, over considerable

periods of time, by overwhelming the system with toxic products (tumor toxins), thus, in some cases, hastening death.

(9) That the injections are often painful, and patients many times refuse to take them.

(10) That the so-called "trypsin abscess" proved, upon examination of the material, to be unabsorbed injectio trypsini plus broken-down tissue.

(11) That when real abscesses formed they were due to faulty technique, to localization of a general sepsis resulting from the absorption of toxic products, to an accompanying sepsis of whatever origin, or to a complicating acute infection.

(12) That injectio amylopsini seems to diminish cachexia in some cases, in accordance with the claims of Beard and others.

(13) That in some cases there was no reason to believe that injectio amylopsini exerted the action claimed for it.

(14) That when amylopsin was injected directly into the indurated area left after injecting trypsin, absorption of the trypsin solution was not hastened.

(15) That 100 minims daily of the "Quadruple X" solution, the strongest made, were given in some cases with no untoward effects.

(16) That improvement in hemoglobin (5 to 12 per cent.) during the first few weeks of trypsin treatment occurs in about one-sixth of the cases examined. In only one-third of these was the increase ascribable to the trypsin alone.

(17) That a gradual and moderate increase in the number of polymorphonuclear neutrophile cells was noted during the first two weeks of the trypsin treatment in a few of the cases.

(18) That with the exception of two cases such leucocytosis as was noted was attributable to the occurrence of complications during the first two weeks of trypsin treatment.

(19) That in fifteen out of the twenty-two cases above mentioned a steady increase (6 to 12 per cent.) in the number of eosinophile cells was noted while patients were on the trypsin injections. There was no eosinophilia in the control cases, nor in the cases treated by trypsin given by the mouth.

(20) That eosinophilia occurred regularly in cases of carcinoma involving the bones or the intestines, even without the exhibition of trypsin.

(21) That the claims for eosinophilia as a test have not been substantiated in our experience.

(22) That albumin and casts were found in the urine before treatment was begun in two cases. In neither of these was the amount of albumin or the number of casts increased at any time throughout the continuation of the trypsin injections.

(23) That in severe cases in the very last stages of the disease hyaline, granular, few pus casts, and occasionally albumin, made their appearance.

(24) That in two other cases in which it was impossible to obtain specimens of urine before beginning the treatment, albumin and casts were present when the cases came under examination; and as the trypsin doses were increased the amount of albumin and the number of casts were increased.

(25) That dextrose was at no time found in any of the urine specimens examined, not even when untoward manifestations of trypsin were present and large doses of amylopsin were being given.

(26) That the series of experiments which were conducted for the purpose of ascertaining the presence or absence of an enzyme in the urine with properties of digestion similar to trypsin, showed the presence of such an enzyme body (irregularly present)

in (*a*) trypsin treated cancer cases; (*b*) noncancerous untreated cases; (*c*) cancer cases which had not received the trypsin treatment.

(27) That the exact constancy of this enzyme body in the urine with reference to the treatment was not ascertained. No enzyme body was found in urines in which there was ammoniacal decomposition.

(28) That the enzyme treatment as administered in the cases herewith reported and according to the suggestions of Dr. Beard, plus important details of regime, does not check the cancerous process.

(29) That it does not prevent metastasis.

(30) That it *does not cure cancer*.

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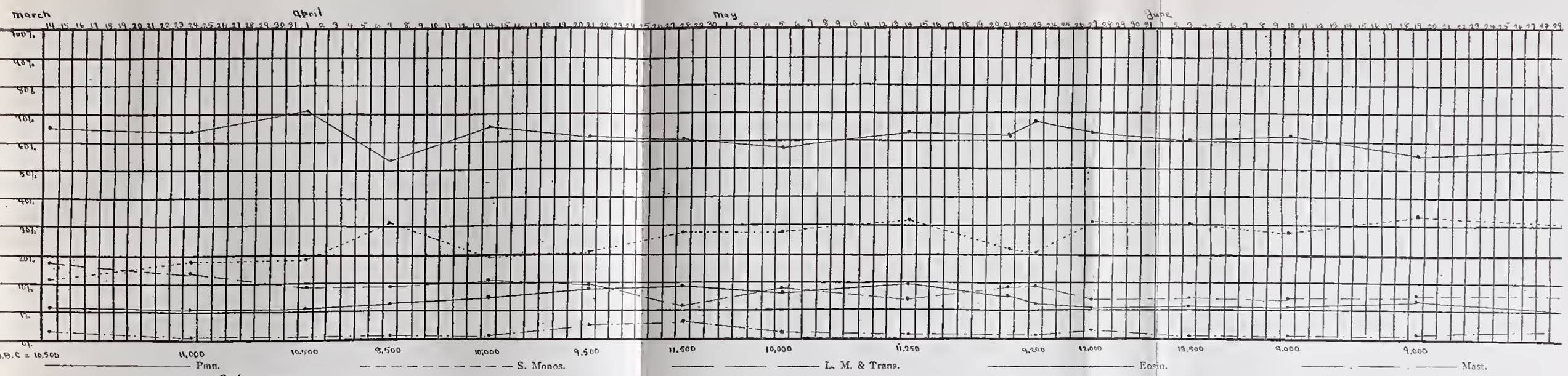

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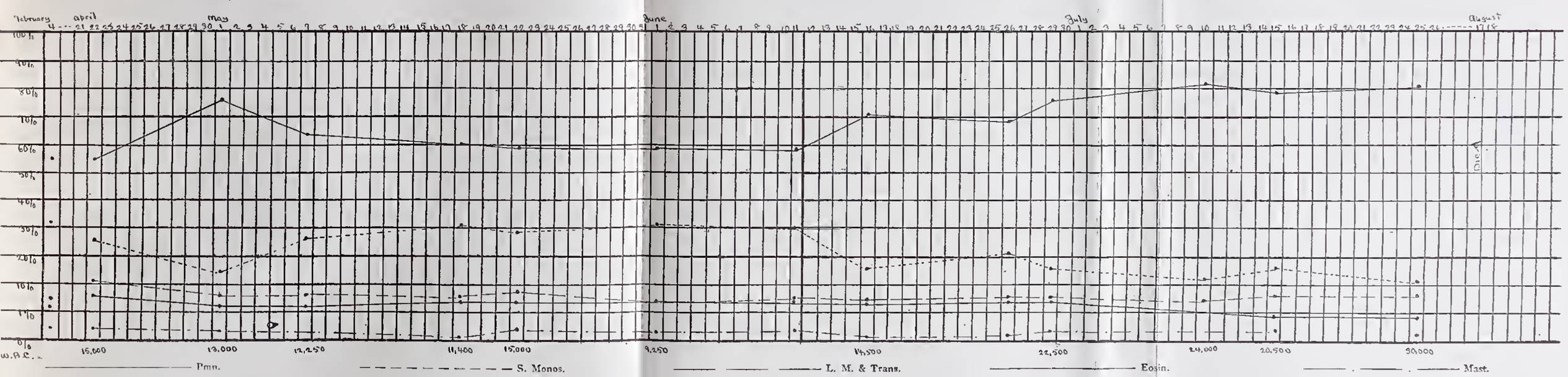

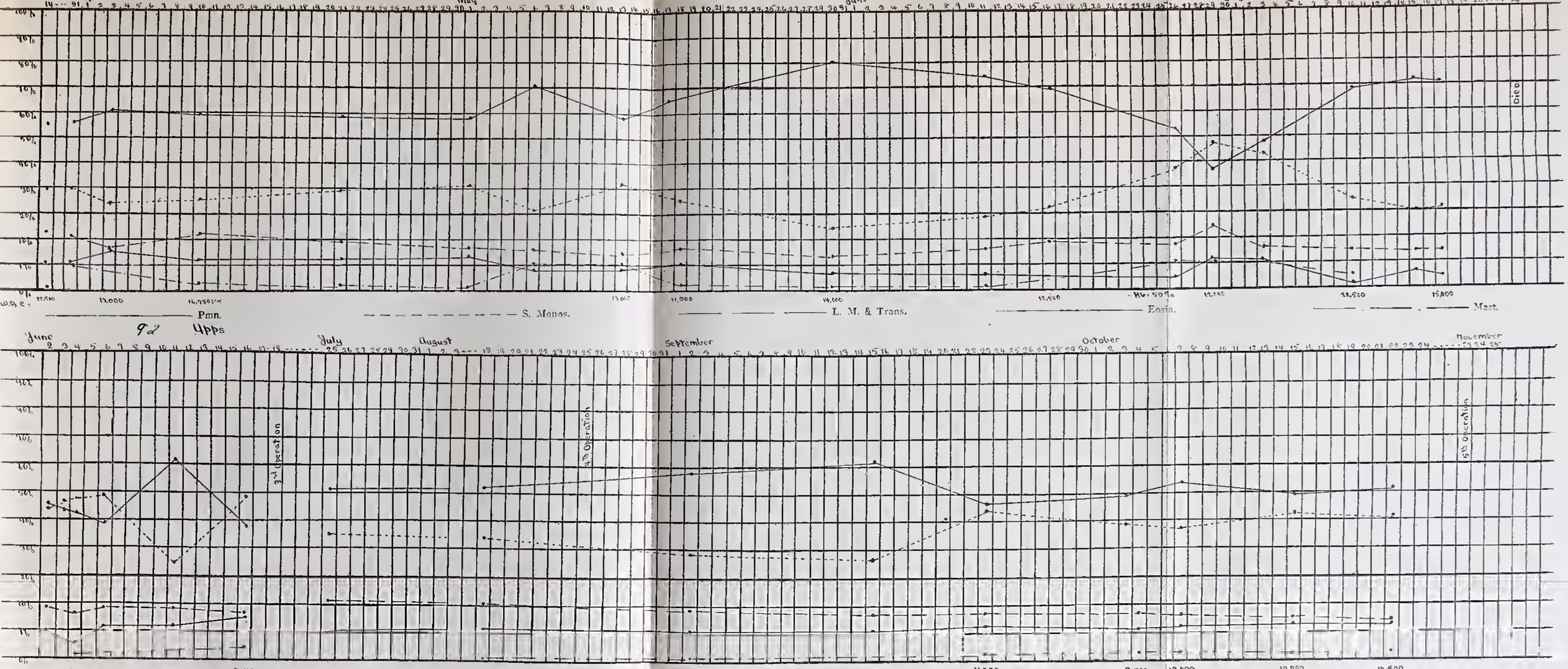

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